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CONTRIBUTIONS TO MEDICAL & BIOLOGICAL RESEARCH

◆

VOLUME ONE

W. Osler

CONTRIBUTIONS TO MEDICAL AND BIOLOGICAL RESEARCH

DEDICATED TO

SIR WILLIAM OSLER

BART., M. D., F. R. S.

IN HONOUR OF HIS SEVENTIETH BIRTHDAY JULY 12, 1919

BY

HIS PUPILS AND CO-WORKERS

VOLUME ONE

NEW YORK
PAUL B. HOEBER
M CM XIX

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Printed in the United States of America

PROEM

My Dear Colleague:

The stealthy foot of Time carries us from youth to age so imperceptibly that we are hardly aware of the change; insensibly we shorten our arms, husband our strength, and are willing to think our prowess undiminished. Yet men have not refrained from marking the lapse of time by signal days, and months, and years; often by celebration of those whose lives have been devoted to the good of their kind, often by memorials of joy and achievement, or again of bitter and unforgotten sorrow.

And, as for the nation or the race, so, in his own life, are there for each of us memorable days of sympathy in joy and sorrow. One day of sympathy in joy was that in the summer of 1904, when some of us were gathered around the hospitable hearth of Sir John and Lady Burdon-Sanderson, and, as suddenly, I believe, to you as to the others of us, like a flash of light the thought was born, how, one scarcely knew, that you might surrender your great functions at Baltimore to enter upon a new life at Oxford.

Ever in the heart of the folk of the New World lies warm and deep the kinship with the old home; thus, almost with the rapidity of thought, between Canada, the United States, and Great Britain an academic link three-fold was forged. In no person as well as in your own could this unity have been so happily consummated; you arrived indeed from overseas but as a pilgrim child of Oxford. In you the literary and historical tradition of the beautiful city was united with the

zeal and adventure of the New World; so that in winning you for Oxford, and for Cambridge and Great Britain, we did no robbery to Baltimore and Montreal.

Since that day we have shared, in our degrees, your happiness and your sadness; we have rejoiced in your honours, and on this day, when you reach the limit that the men of old regarded as the last ripeness of a man's life, I, your brother Regius Professor, am permitted to offer to you from both worlds, as a tribute of admiration and affection, our little horn, if not of plenty, yet of the best of our gardens.

Your "radical humours contain more than sufficient Oyl for seventy years"; oyl enough to keep your lamp trimmed and bright till the old world, now tardily procreant, be brought again to the birth. Meanwhile, in good days or evil, you can thankfully say after our great Example—"My Father works hitherto and I work."

Affectionately yours,

CAMBRIDGE, July, 1919

EDITORIAL NOTE

THE plan to publish a volume in honour of Sir William Osler's seventieth birthday originated among friends in Oxford, Baltimore, and Washington, and the work of organization and of securing papers and subscribers has been carried out mainly by the members of the Committee in those cities.

I was asked to look after the terminal work of putting the copy through the press. This has been made easy through the zealous co-operation and efficient equipment of the publisher. As the members of the Committee are too widely scattered to prepare a collective statement as to their work, I venture to say for them that there was a prompt and enthusiastic response to their appeal for contributions, so that what was planned to be a single volume of modest size has developed by pressure of material into two distinctly large volumes. Even with this expansion many contributions had to be refused because we had reached the limit of time.

In addition it should be recorded here that a number of Sir William Osler's friends were unable to contribute articles on account of the exigencies of the war and the demands made upon them by its conditions.

It was the policy of the Committee to have these volumes made up of scientific contributions, with as little as possible in the nature of personal tribute. The Committee has been fairly, but not entirely, successful, in securing this end. Apart from these personal touches, we believe the subscribers and readers will agree that these two volumes contain a really amazing variety of sound contributions to medical and bio-

logical science. We hope that the collection will be found to justify the Committee in the work it has expended, and that its merits will do proper honour to the character and services of the friend whom these records celebrate.

C. L. D.,
For the Committee.

July, 1919.

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THE OXFORD UNIVERSITY MUSEUM

By T. D. Acland, London

NO birthday greeting to Sir William Osler would be complete without some message from the University Museum, the foundation of which was so largely due to one of his predecessors in the Chair of Medicine, which he so worthily occupies.

My only excuse for attempting such a task is that there are very few Oxford graduates now left who have had so long an association with the building, and with those who bore the brunt of the battle which ended in the recognition of scientific teaching and research as a part of the university education.

I knew the spot on which the museum now stands when it was a ploughed field, and from my childhood have been acquainted with those whose names will, for all time, be associated with the struggle for those scientific and artistic ideals which are represented by the material fabric.

It was originally my intention to have written some account of the museum and of those associated with it in its earliest days, but the countless inevitable interruptions in a life made busy by the aftermath of war has made this impossible. Rather than give it up altogether I have ventured to send two short sketches as a small contribution to the record of the building whose foundation has meant so much for Oxford. One deals mainly with the ideals for which the museum was built, the other recalls certain incidents in the erection of the building which have always attracted me.

I am also sending some illustrations which may be of interest. The original drawing of the keystone of the arch, of which I give an account, is in my possession, as well as the bust of Mr. Ruskin and the portraits of Sir Henry Acland and Sir John Burdon-Sanderson.

I cannot close this brief introduction without saying what I owe to the encouragement of Dr. Singer; if it had not been for his ready help and enthusiasm I should not have had this opportunity of sending any greeting to one to whom Oxford is so greatly indebted. Such as it is, I beg that it be accepted as an expression of my admiration for Sir William Osler's great work in the encouragement of scientific medicine, and of his devotion to those principles of medical education for which the builders of the museum fought so courageously.

"LITERÆ—SCIENTIA—PRAXIS"

So runs the legend inscribed beneath the portraits of three distinguished sons of Oxford in the Regius professor's room at the University Museum.[1] The portraits were a legacy from Sir Henry Acland, one of the leaders of that far-seeing band of pioneers who were able to look forward in faith to the time when scientific teaching and research should occupy their proper place in the university. The words express his ideal of what should be the proper relation of Oxford to the teaching of science. In urging the need for the building of a central institute he expressed the fear that unless some place was given where the study of the natural world in the university could be carried on, *in addition to* the philosophic studies of the past, Oxford might see what would be a great national evil—namely, the *substitution* of Science for Letters and Philosophy, instead of a *combination* of the two (for which he hoped), greatly to the detriment of sound education. The function of the Oxford Museum, he wrote, after the building was complete, "is to train good scientific observers and thinkers to become observers and thinkers in Pathological, Therapeutic, and Preventive processes. They will then, I hope, enter the vast field of disease which is seen in the great hospitals of the metropolis as broadly educated and

[1] The portraits are those of Linacre, Harvey, and Sydenham. Linacre was a Fellow of All Souls in 1484. Sydenham was at Magdalen Hall, and became a Fellow of All Souls in 1648. Harvey, it may be objected, was a son of Oxford by adoption only, as he was a graduate of Cambridge. He was Warden of Merton in 1645.

Oxford University Museum, 1860.

really thoughtful men." To-day these words are so like a truism, which everyone admits, that it is difficult to realise the strength of the opposition and the apparent hopelessness of the attempt to effect the change from the old order to the new.

Nothing can show these various opposing forces with such clearness as the actual words of prominent men in the university—some in reality sympathetic, though hopeless, others wholly antagonistic. Of these certainly the most remarkable is the reply given by Dean Buckland, Reader in Geology and Mineralogy in the university. When asked in the year 1847 to join Daubeny, Walker, Acland, and others, in a memorandum stating that in their opinion there was need for the erection of a building for the better display of materials illustrative of the facts and laws of the natural world, he wrote:

"Some years ago I was sanguine as you are now as to the possibility of natural history making some progress in Oxford, but I have long come to the conclusion that it is utterly hopeless. The idle part of the young men will do nothing, and the studious portion will throw their attention into the channel of honours and profits which can alone be gained by the staple subjects of examination for degrees and fellowships.

"At present it is a detriment to a candidate to have given any portion of his time and attention to objects so alien from what is thought to be the proper business of the university as natural history in many of its branches. I therefore return the paper, which I think it useless mockery to sign. . . ."

Such was the reply from the man of science. But this rebuff, crushing as it must have seemed, was not the worst. Dr. Pusey, the great theologian, whose influence in the university was at its height, in answer to a question by the recently appointed Lee's Reader in Anatomy at Christ Church, as to whether he and his friends seriously discouraged the study of natural science, replied, "It is so. We notice that it engenders in those we know, a temper of irreverence and often of arrogance, inconsistent with a truly Christian character." But to his infinite credit in reply to further questions, he said: "The desire to possess such knowledge and the power to attain to it are alike the gift of God. They are to be used as such: while you discharge your duties in that spirit you may count on my assistance whenever you need it." That promise was loyally fulfilled. Dr. Pusey's influ-

ence was, later on, invaluable to those who were struggling for the erection of the museum, and at one critical period was the determining factor in the struggle.

There is no need to say more as to the variety and complexity of the forces ranged in opposition to the recognition of science in the university in the early days before the museum was built, but a most interesting side light is thrown upon the state of opinion in Oxford by a letter of Professor Jowett's written in 1884—some years after the museum was built—when the objects for which it was founded had long been recognised as essential to the university.

"It seems to me that all those who like ourselves are entrusted with the care of ancient studies have a hard battle to fight against the physical sciences, which are everywhere encroaching, and will certainly lower the character of knowledge if they are not counteracted. All the higher conceptions of knowledge and of the mind will be overwhelmed by the immediate and sensational and the sentimental *et hoc genus omne*. Physical science and art, against morals and religion and philosophy and history and languages. I am not an alarmist, but am inclined to think that unless we all unite, the 'repulsive' persons who will only believe what they can hold in their hands will be too much for us." (1)

How far it was from the wishes of those who were mainly instrumental in founding the museum, to oppose science to philosophy, may best be gathered from the concluding words of the preface to the first edition of "The Oxford Museum," written in 1859:

"The further my observation has extended the more satisfied I am that no knowledge of *things* will supply the place of the early study of letters—'Literæ Humaniores.' I do not doubt the value of any honest mental labour. Indeed, since the *material* working of the Creator has been so far displayed to our gaze it is both dangerous and full of impiety to resist its ennobling influence even on the ground that his *moral* work is greater. But notwithstanding this, the study of language, of history, and of the thoughts of great men, which they exhibit, seems to be almost necessary (as far as learning is necessary at all) for disciplining the heart, for elevating the soul, and for preparing the way, for the growth in the young, of their personal spiritual life: while, on the other side, the best corrective to pedantry in scholarship, and to conceit in mental philosophy, is the study of the facts and laws exhibited by Natural Science." (2)

The situation as it appeared to an outsider is well given in Mrs. Humphry Ward's "Recollections of Oxford in the Seventies."

"Balliol, Christ Church, Lincoln, the Liberal and Utilitarian Camp, the Church Camp, the Researching and pure Scholarship Camp, with Science and the Museum hovering in the background as the growing aggressive powers of the future seeking whom they might devour. They were the signs and symbols of mighty hosts, of great forces still visible, incarnate and in marching array. Balliol versus Christ Church, Jowett versus Pusey and Liddon, while Lincoln despised both, and the new scientific forces watched and waited."

It was amidst such rival and contending parties that the museum came into being, aided and loyally supported by Pusey, Liddell (Dean of Christ Church), Jacobson (afterwards Bishop of Chester), Stanley (afterwards Dean of Westminster), Thompson (afterwards Archbishop of York), Wilberforce (Bishop of Oxford), and many others, who saw no antagonism between the reverend study of nature and the learning of those ancient philosophies and creeds to which the university so far had been almost wholly devoted. Much more might be written of the opposition to the erection of the building, to which one learned divine always alluded as the "cockatrices' den"; but enough has been said to show the temper of the age in which the work was brought to a successful issue.

NISI DOMINUS ÆDIFICAVERIT DOMUM

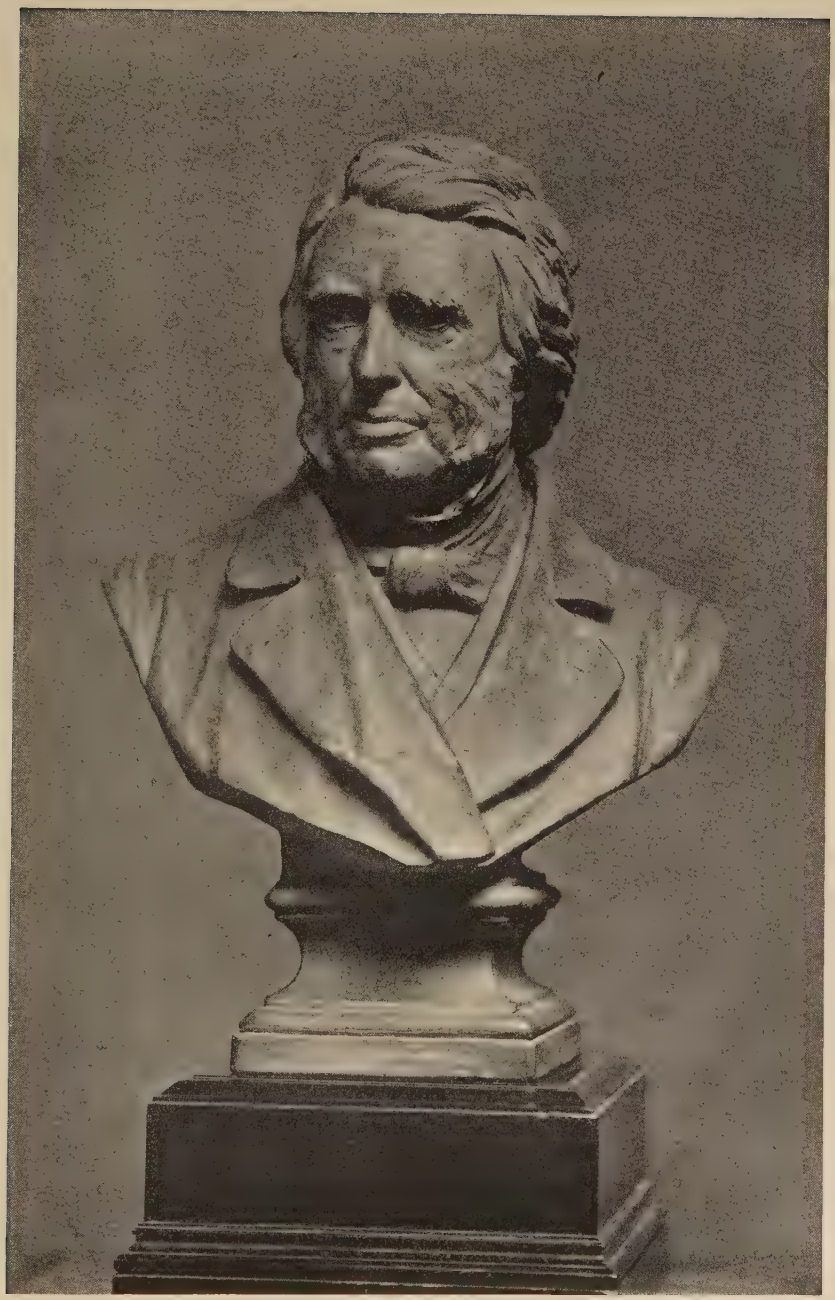
Such was the motto sent in with the design in Rhenish Gothic for the new University Museum by Benjamin Woodward, whose early death was a grievous loss to British art.

This is no place to enter into any discussion as to whether Gothic was the best style of architecture for the new building. At any rate, Ruskin, in his enthusiasm, had no doubt about it. He lays it down (3) "that all seriously purposed defenders of Gothic architecture are convinced that the essence and power of Gothic, properly so called, lies in its adaptability to all need." He goes on somewhat humorously to argue that if "pillars or piers come in your way when you have to point, or vaults in the way of your voice when you have to speak, or mullions in the way of your light when you want to see, just so far has the architect failed in expressing his own principles or those

of pure Gothic." There is no question as to the beauty of much of the work, and as to the adaptability of the original building to the purposes for which it was designed—that is: to be the nucleus of many other buildings spreading around it.

It has always seemed to me that the archway over the main entrance, designed by Pollen and partly, it is believed, carved by Woolner, gives in its present state an epitome of the hopes and fears with which the museum was founded, and more than this, that it bears eloquent witness to the struggles, disappointments, and delays with which the work was surrounded before at last it was brought to a successful end. On the keystone of the arch there is carved in low relief the figure of an angel; in his right hand he holds an open book, in his left he carries three dividing cells, emblems of life and of all living things. This figure is an expression of the intentions of those who strove for the foundation of the museum in the hope that future generations might there have the opportunity of studying the book of nature, and of searching out the mysteries of life, guided by a higher power who alone could give them understanding to read aright the pages of the book laid open before them. It is significant that on the open pages of the book there are as yet no words written, as though to show that he who would search out the secrets of Nature must make the record for himself.

On either side of the arch is seen a human form, type of the highest of all created things. The man is holding in leash a bloodhound, the symbol of material death; on the other side, a woman with the serpent, foretelling sin and its consequences; from these two an interwoven mass of flowers and fruit and thorns spring up to reach the summit—a symbol of the unceasing struggle between happiness and sorrow, good and evil, right and wrong, pleasure and pain, which accompany us through life until the end. This is not all. On the lower edge may be seen on the right-hand side a line of ill-defined forms, roughly cut out in stone, and there left unfinished and incomplete. If it be true, as Ruskin says, that the "highest art in all kinds is that which conveys the most truth," then it may truly be said that this unfinished arch is an expression of the highest kind of art, for it is a sagacious—even though somewhat bitter—comment by the sculptor on those who by their opposition delayed the work of building the museum, and showed by their useless talk how little

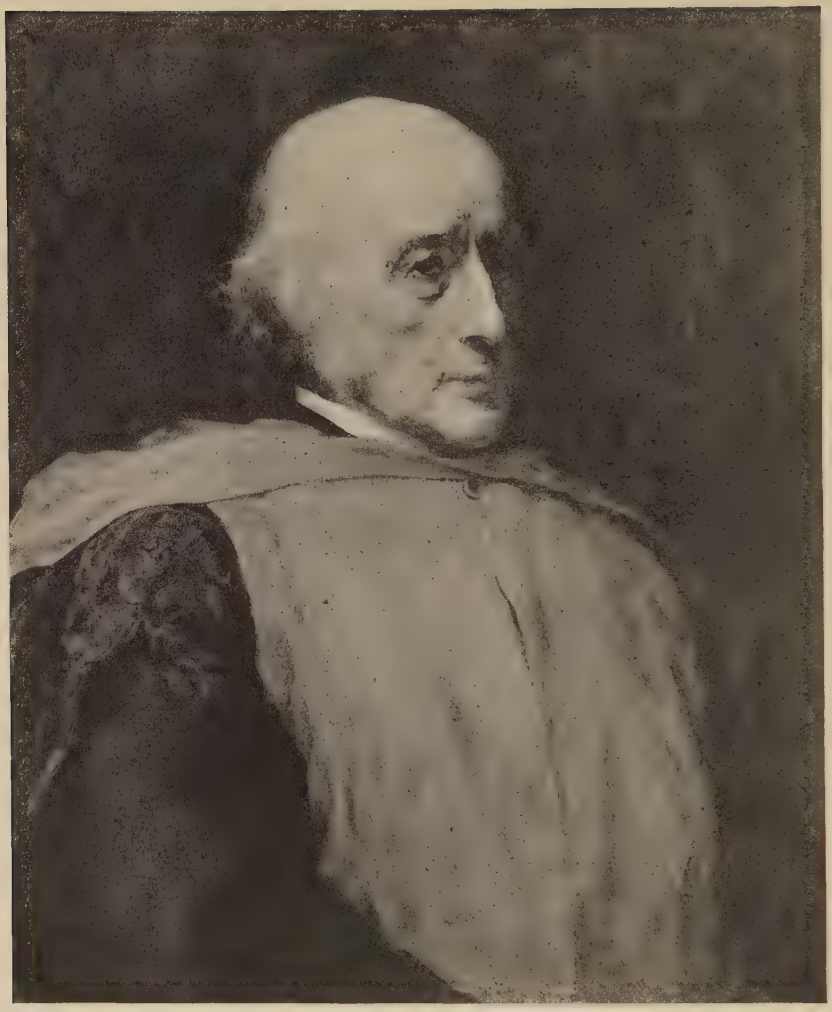


JOHN RUSKIN, 1819–1900.
Professor of Art at Oxford, 1870–1879.
From the Bust by Sir E. Boehm.

Main Archway, Oxford University Museum.

DESIGN FOR A WINDOW IN THE MUSEUM.
From a Sketch by John Ruskin.

CAPITAL OF COLUMN.



Henry Wentworth Dyke Acland (Æt. 81), 1815–1900.
Lee's Reader in Anatomy, 1845. Regius Professor of Medicine, 1858–1894.
From the Portrait by W. W. Ouless, R.A. (1896).

they understood the aims of those who had designed the fabric. Those ghostly forms are no part of the original design. Their story is as follows:

There was employed in the museum a stone-carver—an eccentric genius named O'Shea, whose carving on some of the capitals, representing the natural orders of plants, excites the admiration of all who see them. One day he was carving the arch of one of the Gothic windows, the cost of whose decoration had been undertaken by Mr. Ruskin, when he was hailed by the Master of University College. "What are you carving there, Shea?" "Monkeys, your honour; I'm carving the Darwinian theory." "That can't be allowed," retorted the indignant delegate; "we can't have monkeys climbing up the museum windows; you must have them out." Next day he came along to see that his order had been obeyed, and seeing Shea at work, called out, "Why, Shea, you have not done as I told you; what are you carving now?" "Cats, your honour. They are cats to-day." At the moment there was no reply. The "catamonkeys," as these strange attenuated beasts came to be called, may be seen to the present day, crawling round the second window of the first floor on the right of the central arch, presenting forms unknown to natural history, and attesting equally to the skill of the carver and the disfavour in which at the time the Darwinian theory was held by one of the leaders of thought in Oxford. At a later period, when the available funds had been exhausted, and a parsimonious or indigent university had decided not to spend a penny more on "those useless decorations," Shea was dismissed. He was angry with a righteous and Celtic anger, and was found next day working (as he had seldom worked before for pay) at the great central archway, which was still unfinished. Here he was found by Henry Acland with the chips flying fast and furiously round him, moulding out a row of heads along the lower margin of the arch. "Hullo, Shea," says Acland, "I thought you had been dismissed." "So I have, your honour," he replied, redoubling the energy of his work. "Well, but you know you won't get any pay for this." "I know, your honour; it's all right." "But what are you carving?—Owls and parrots!" "Owls and parrots, your honour—heads of houses and members of Convocation."

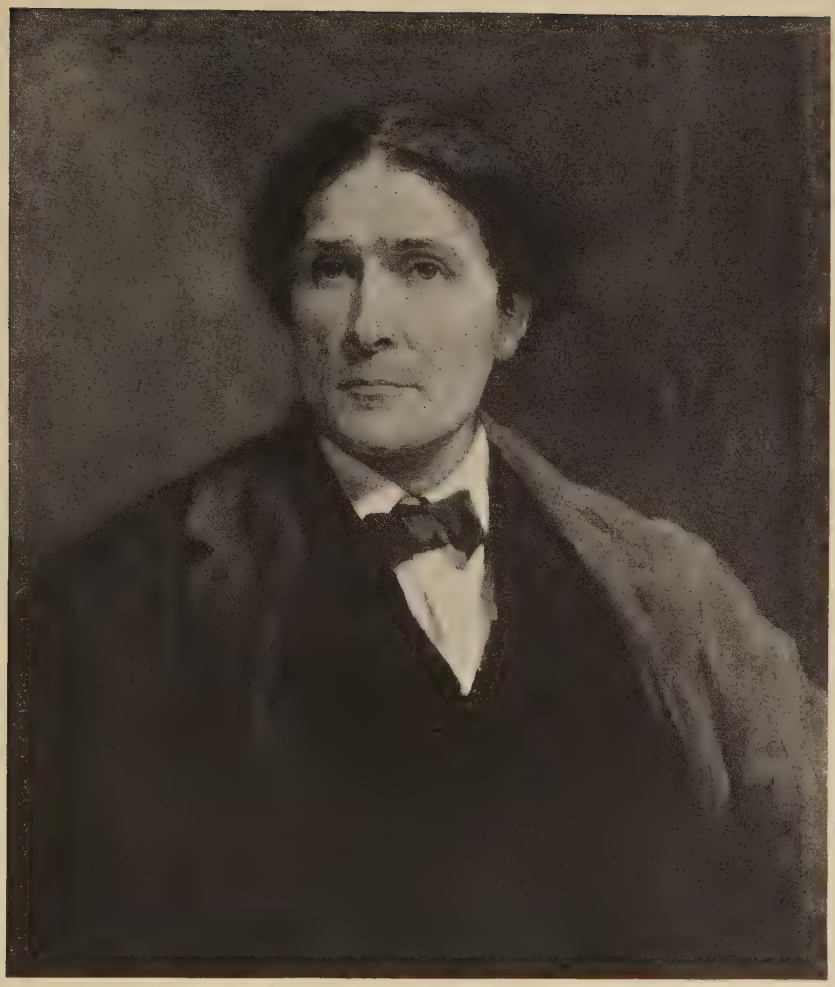
And there they are, roughly moulded and defaced in obedience to peremptory orders, but none the less an eloquent testimony

to the vexatious delays and obstructive tactics which were sufficient to exasperate even the workman to such a pitch as to goad him to work for nothing. Who shall say that he did not have his revenge? Such episodes, trivial as they are in themselves, tell eloquently of the struggle which was carried on to establish the new teaching; a struggle which, however protracted, was at last to end in victory.

The building was to be an institution round which were to be centred all the various departments needed to investigate and teach the great truths of Nature. All that concerns man and his dwelling place was to have a home there; all that shows the relation of this earth to the infinite universe around was to be studied, all that affects man in health and disease. Each was to have its appropriate laboratories, classrooms, and museums, and the central point was to be a great library in which might be stored the best that all the greatest minds had contributed to our knowledge of the material universe; so that the whole order of creation should be represented in such a way as to make it intelligible to the student and give him opportunities of study in whatever direction he might wish to direct his enquiries. It was a fine conception of a noble ideal, and possibly, had funds been generously provided, might have been carried out more speedily and with more elaborate detail. Much, however, has been done, and the great efforts which were needed to get the various departments organised and started have been more than repaid by the value which is placed upon them now that they have at last been erected and equipped.

Since the opening of the museum, in 1858, ten new departments have been added, and the Radcliffe Library has been housed in a new building. The names of these, and the approximate dates on which they were built, are given below:

1. Clarendon Laboratory (Physics). 1872.
2. Physiological Department. 1884.
3. Pitt-Rivers' Museum. 1884.
4. Human Anatomy. 1891.
5. New Radcliffe Library. 1901.
6. Pathological Department. 1901.
7. Morphological Laboratory. 1901.
8. Electrical Department. 1910.



JOHN BURDON-SANDERSON, 1828–1905.
Waynflete Professor of Physiology, 1882–1895. Regius Professor of Medicine, 1895–1905.

From the Portrait by W. W. Ouless, R.A. (1886).

9. Engineering Department. 1915.
10. New Chemical Laboratory. 1916.

Of the portraits, two—one of Sir Henry Acland, the other, of Sir John Burdon Sanderson—(his successor in the Chair of Medicine)—are from the paintings by W. W. Ouless, R.A., that of Ruskin is from the bust by Boehm. I have preferred these to others since they are less known than many which have been previously published, and they have therefore an added interest.

The photograph of the museum, the capital, and other architectural features I owe to the kindness of Professor Bowman and the delegates of the museum. The photograph of Mr. Ruskin's design for one of the windows was lent me by Miss Acland (of Oxford). To all of these I wish to express my thanks; without the kind help which I have received from them and other friends, it would have been impossible for me to have given these illustrations, which I cannot but feel add a value to my two brief sketches which they could not otherwise have possessed.

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3. Letter in "The Oxford Museum," 45.

ON THE PROBLEM OF GRADUATE MEDICAL STUDY IN LONDON

By J. G. Adami, M.D., F.R.S., F.R.C.P., F.R.C.S.,
Montreal, Canada

IN these latter days, when the patron of letters and of men of letters no longer exists, and with his departure from the scene there has departed the need to recognise his largesse, the dedication of a volume is no longer a necessity, but a luxury. It has become a spontaneous or free-will offering, and as such is apt happily to disclose the soul of the author.

There are few of us medical men to whom the dedication of Osler's "Medicine" does not appeal:

TO THE

Memory of my Teachers:

WILLIAM ARTHUR JOHNSON,

PRIEST OF THE PARISH OF WESTON, ONTARIO.

JAMES BOVELL,

OF THE TORONTO SCHOOL OF MEDICINE, AND OF THE UNIVERSITY OF TRINITY COLLEGE, TORONTO.

ROBERT PALMER HOWARD,

DEAN OF THE MEDICAL FACULTY AND PROFESSOR OF MEDICINE, MC GILL UNIVERSITY, MONTREAL.

We know full well that what we have accomplished and what we are depend largely upon the influence of certain of our old teachers. They it is who carried on the flame, lighting, or tending, the light that is within us—such as it is.

As a member of the Faculty of that school in which Sir William gained his training in clinical medicine, in which he held his first chair, in which, indeed, it pleases me to think that a fourth part, or

so, of his mantle, when he was called higher, eventually fell to me,[1] there would have been a certain appropriateness had I, in these pages, traced the influence of the great Montreal teacher, commemorated in that dedication, upon Osler and upon his generation in Canada. For his influence was great, and like that of those others who have depended more upon the spoken than the written word, its memory is apt to fall into oblivion. But Palmer Howard had been dead some few years when, in 1892, I came to McGill, and the notes that I have taken from time to time regarding his method of teaching medicine, the extent to which those methods pervade the great text book, and the impression he made upon his students would need to be amplified by correspondence with his old pupils and others in Canada; and with me here in London and not in Montreal, time forbids.

There is, however, another line of thought called up by that tripartite dedication, namely, the debt owed by Osler and other scholars in medicine, as in other branches of knowledge, to their wanderings from school to school. And this leads inevitably to the insistent problem of graduate teaching.

Stationed as I have been in London throughout the war, the more special case of the larger problem naturally occupies the foreground. The case may be placed thus: The larger the amount of material passed in review the greater the experience to be acquired, and the greater the grasp. Here, in the largest city in the world, the student in medicine should find the greatest wealth of material of all orders collected, not merely from London itself, but from the British Isles and indeed, as at Greenwich, from all parts of the world. Here, then, should be the greatest opportunity for advanced study: London should be the natural centre for the graduate study of at least the English-speaking world, if not of the world in general, surpassing Vienna, Berlin, and Paris in her attractions as a medical centre, just as she exceeds them in population. It is proper that the centre of the British Empire should be the centre for the medical men of the Empire.

Now, notoriously, this has not been the case in the past. With certain exceptions to be presently noted, the graduate student of

[1] For the "Institutes of Medicine" of the curriculum of the "eighties" is to-day represented by the departments of Physiology, Histology, and Pathology, if not also, as regards physical signs, by that of Clinical Medicine.

medicine has during the greater part of the last hundred years shunned London. The vast majority of North American graduates, both of the United States and of Canada, have of late pursued their studies in Germany and Austria, of Central and South America in Paris. And if we seek the cause from those of our students whom we have encouraged not to follow in the footsteps of the crowd, we find that, with the exception of those who have devoted themselves to the specialties, the constant complaint is that such opportunities as are afforded—and afforded by many teachers with the greatest of willingness—are neutralised by imperfect organisation of graduate, or "post graduate," instruction. (The "post" I hold is redundant and should be cast out.) One and all complain of the hopelessness and weariness of the wandering from hospital to hospital across the great city, the painful loss of time, the frequent disappointment engendered by failing to make the time-table fit in, and by only managing to arrive at this or that lecture or demonstration twenty minutes to half an hour after it has begun.

I have been told this again and again with bitter regret. It is, I would emphasise, equally true that there is no city in the world in which the young English-speaking graduate of medicine—I speak for the Dominions—finds himself more interested, of which he more desires to be a temporary citizen: none that exerts a greater attraction. He knows the wealth of material that is here, if only he could use it. He knows that in part through the natural attraction exerted by London, in part through the intense competition between the many schools, there exist here in London many of the acutest physicians, surgeons, and specialists of the English-speaking world.

Can the problem be solved? As one observing from outside, it may be serviceable if I put down certain considerations and conclusions which I hold must be taken into account for a right solution.

I. The only students who thus far have been completely satisfied with their graduate work in London are those who have confined themselves to a single specialty, or to the work and opportunities afforded by a single hospital. I have, for example, heard nothing but enthusiastic commendation from those who have come to London for ophthalmology and have attached themselves to Moorfields; for diseases of children, and have attended at Great Ormond Street; from neurologists gaining entrance to Queen

Square. Surgeons and physicians who have come to London with the special object of placing themselves under one of the great surgeons or physicians of one of the large general hospitals have, in general, obtained an abundant reward.

II. It is useless to offer, as has been attempted in the past, a weekly curriculum of lectures and demonstrations at all the leading hospitals, and to encourage graduate students to take as many as possible of these courses.

III. It is a serious mistake to offer courses of lectures to graduate students at medical schools and the hospitals therewith associated, devoted to the training of undergraduate students, by those engaged in the teaching of the said undergraduate students. If the courses of lectures and demonstrations are special, for graduate students only, these find the lecturers already worn out by their undergraduate courses. If the courses are common to graduates and undergraduates, the presence of the former and their occupation of the front seats place the undergraduates at a disadvantage and are harmful to the school.

IV. It is, therefore, a mistake to have the graduate teaching in London controlled by a committee of leading physicians and surgeons, attached, as is almost inevitable, to the leading medical schools. Most naturally those leaders want their particular schools to cater for and attract the best of the graduates; if a rival school has particular attractions, they find it difficult to admit that their own school cannot offer the same, and are apt to arrange and advertise courses which are not the best.

V. Thus, pending the establishment of a University Hospital, devoted to the promotion of research in clinical medicine and surgery, and properly staffed with full-time professors in medicine and surgery, with full-time assistants, certain of whom could undertake the training of graduate students, it would be better to confine graduate teaching in London to hospitals which are not already the seat of medical schools. As things are at present there is a great opportunity for the provincial schools—Edinburgh, for example, Manchester, and Glasgow—by appointing full-time assistants to the important chairs, to cater for graduate students from overseas. They have the advantage of having their teaching facilities concentrated.

VI. If there is no immediate prospect of the establishment of such University Hospital in London, it would be excellent policy on the part of one or more of the existing hospitals to which is attached a redundant medical school for undergraduate students, to convert itself into a school for graduate studies, and for large general hospitals which have no undergraduate school to adopt the policy of attaching to themselves rising physicians and surgeons of the first order and to develop themselves into graduate schools.

VII. From the experience of the last thirty years it is abundantly evident that a committee of representative members of the profession in London is incapable of establishing a live graduate school. The supply may suggest, but does not determine the demand; on the contrary the demand creates the supply. The eminent success of Vienna as a graduate school for those from the United States and Canada in this generation has been due to the existence of a bureau, represented, I believe, largely by one man, a United States medical graduate who, through his intimate knowledge of medical matters in the Austrian capital, was able to advise the student, on the one hand, to the best advantage and, on the other, from his control of the student material, to arrange for those courses being given, not which are most convenient for the staff to offer, but which are most needed by the student. I can foresee such a bureau in London, at which all medical graduates desiring graduate work would register themselves; where they would state the nature of the course or courses needed, and the head of the bureau would make arrangements for them to obtain those courses; where, instead of the graduate paying fees to each hospital, a single fee, say of £12, 10, 0 each quarter, would cover the costs of registration and running the bureau, and of hospital fees. Tuition fees, from junior members of the hospital staffs, would be extra according to an arranged scale—a given sum for individual tuition, a lesser sum where two, three, or more graduates received instruction in common. Fees for laboratory courses also would be extra. It might be possible and profitable to charge a smaller fee, but were it £12, 10, 0 (fifty dollars), then one-fifth of this would be employed for bureau expenses. If the graduate attached himself to one hospital, and put in all his time there, £10 would be paid by the bureau per quarter to that hospital; if to two or more, then

the £10 would be divided among them in the proportion of the time arranged to be spent in each. The graduate would be given a card for the quarter, which would constitute his credentials, and a Committee of Management representative of the hospitals would audit the accounts and oversee the administration of the fund.

Such a bureau, working primarily on behalf of the medical graduates, and not of the hospitals and their teaching staffs, would best formulate and secure the fulfilment of the graduates' needs.

It is along these lines, I feel convinced, that the problem is to be solved. What is more, we have established in London at the present moment what might serve as the basis for such a bureau. I cannot speak for the Australasian and South African graduates, although once a bureau was established these would easily fall into line, but on the one hand students from the United States are represented by the body which, under Dr. McLean (late president of the University of Iowa), is looking after the interests of soldiers from the Statesian Universities at present in this country, with headquarters in Pall Mall, and on the other the "Khaki University" under President Tory of the University of Alberta is charged by the Government of the Dominion of Canada with arranging with British Universities and technical schools for the establishment of courses of instruction for duly qualified members of the Canadian Expeditionary Force. The United States and Canada have, therefore, taken the first steps along the line here laid down. The question is, which party shall take the next step? Can the Royal Society of Medicine establish the necessary organisation, or better still, the newly created Fellowship of Medicine, with its President, Sir William Osler?

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The above was written in January. In April, when the proof reaches me for revision, the provision of graduate teaching in Great Britain for several hundred officers of the army medical corps of the United States has led to the plan outlined above, being called into being under the continued activities of the Fellowship and of President McLean's American University organization, with a citizen of the United States, a British graduate practising in London, as organizing secretary.

THE OXFORD MEDICAL SCHOOL IN THE EIGHTEENTH CENTURY

By Arnold Chaplin, M.D., F.R.C.P., London

THE Sister Universities were founded for the purpose of affording facilities for the acquirement of every form of learning, and when knowledge concerning any particular branch of art or science became a necessity, a special school devoted to its teaching was established in the Universities. In this way the school of medicine arose at Oxford, and in 1546 King Henry VIII founded five professorships in various spheres of learning, of which medicine was one. Previous to that date, Linacre, ever anxious to promote the knowledge of medicine, had, in the year of his death in 1624, established three lectureships in physic. His executor, Cuthbert Tunstall, Master of the Rolls, apportioned two of them to Merton College, and this may be regarded as the first attempt to recognise medicine as a subject worthy of special attention at Oxford. From the institution of these "Linacre Lectures," however, much advancement in the knowledge of medicine could hardly be expected, for the lecturers, following the slavish adherence to the so-called authority of those days, were required only to explain and comment upon certain parts of Galen and Hippocrates.

After the establishment of the Regius professorship in 1546, further additions to the medical school took place from time to time. In 1617 King James I annexed to the chair of medicine the Mastership of Ewelme Hospital, and in 1624 Richard Tomlins founded a prælectorship in anatomy, which he joined to the professorship. No further bequests designed for the improvement of medicine at Oxford were received until 1714, when John Radcliffe by his will established the "Radcliffe Travelling Fellowships." In 1762 Dr. Matthew Lee founded a lectureship in anatomy at Christ Church for the purpose of giving instruction in that subject to six students of the House who had been educated at Westminster School. The foundation also provided for a dissecting

room and a museum of anatomical specimens. At first a lecturer was specially appointed to deliver these lectures, but soon it became the practice of the Dean of Christ Church to delegate the duty to the Regius professor of physic, and the lectures he gave by virtue of his professorship were admitted as a discharge of the Lee trust.

In 1780 the third Earl of Litchfield, then Chancellor of the University, founded a professorship for the reading of clinical lectures in the Radcliffe Infirmary. The design of this trust, which was not vested in the university, although the professor was chosen by Convocation, contemplated the use of the clinical material in the Radcliffe Infirmary for the benefit of the medical students in the university. But in 1877 the University Commissioners recommended that, in future, lecturers in medicine and surgery should be elected, in place of the professor, to give clinical instruction to members of the university at the Infirmary. In 1883 this change was carried into effect, and since then the lecturers have been chosen from the staff of the institution. The first Litchfield professor was John Parsons, and he was followed by Martin Wall in 1785, Robert Bourne in 1824, James Adey Ogle in 1830, and Henry Wentworth Acland in 1857.

The last of the foundations connected with medicine at Oxford was that of Dr. George Aldrich of Merton College, who established by his will in 1798 three professorships in anatomy, chemistry, and clinical medicine. Dr. Aldrich himself devised the revenues of the professor of anatomy to the Tomlins prælectorship, and, therefore, to the chair of the Regius professor, but since 1877 they have been made applicable to the payment of the demonstrators in anatomy. The professorship of clinical medicine was held by Dr. Bourne in 1803, and he was succeeded in 1824 by Dr. James Adey Ogle. In 1858 the chair was annexed under statute to that of the Regius professor. The chair of chemistry was held successively by Dr. John Kidd in 1803, Dr. Daubeny in 1822, and Sir Benjamin Brodie in 1855, when it was suppressed in the following year.

When medicine emerged as a distinct branch of learning at Oxford, somewhat elaborate statutes were drawn up for the control and guidance of those engaged in its study. In those early days

Oxford and Cambridge were the only places in this country where the study of medicine could be prosecuted, and since at both universities the facilities for medical education were regarded as equal, it was ordained that a graduate in medicine of either could be incorporated at the sister university with a similar degree. In some cases foreign universities were accorded the same right, and the daughter University of Dublin enjoyed the same privilege. Nearly all physicians, therefore, engaged in the practice of medicine in England were graduates of either Oxford or Cambridge. But the charter of the Royal College of Physicians, granted in 1518, introduced a new and legally constituted body with powers to control physicians. By the terms of the charter, all who practised medicine in London and seven miles around were obliged to be licenced by the college, and by a further charter, all who practised in the Provinces were under the same obligation, except those who were graduates in medicine of Oxford or Cambridge. Except in the Provinces, therefore, a degree in medicine from the sister universities conferred no title to practise as a physician. This, however, proved to be no great disability, for at that time no person who did not hold a degree in medicine from either Oxford or Cambridge could become a Fellow of the college.

Until the latter end of the eighteenth century, medical instruction at Oxford did not extend beyond such knowledge as could be obtained from books, and the few lectures on anatomy given by the Regius professor; yet the statutes compelled students to pass the whole of the medical curriculum at the university. When, however, it came to be recognised that a knowledge of medicine embraced practical work which could be obtained at other and better schools in London, Edinburgh, and on the Continent, these strict statutes as to residence were allowed to fall into abeyance, and students were permitted to pursue their medical studies away from the university. They were never in residence, and put in an appearance only to perform the merely formal exercises for the medical degrees. Thus it came to pass that although teachers of medical sciences were established at Oxford, no opportunity occurred for imparting knowledge on account of the lack of students. The fame of Padua and Leyden attracted all those engaged in the study of medicine, and the professors at the universities lapsed into

a state of indolence and ease. But although the teaching of medicine at the English universities was almost a farce, one great principle was strictly observed. No student of medicine could proceed to a medical degree until he had graduated in Arts, and thus a thorough training was secured for all those who contemplated the career of a physician. Whatever may have been the manner in which knowledge of the Arts was imparted, there can be no doubt that it was the intention of those who framed the courses of instruction to give a thorough grounding in the subjects taught. That the instruction in Arts was adequate will be admitted when the long line of erudite physicians proceeding from Oxford and Cambridge is remembered.

However admirable from an academic point of view the Regius professors at Oxford may have been, it must be admitted that, as a body, they could claim little distinction in medicine. Some of them had never studied their subject anywhere except at Oxford, and scarcely any of them had contributed to the special branch of learning over which they presided. Indeed, their duties were so light that residence away from Oxford constituted no bar, and some of them, such as Woodford, Vivian, and Pegge, lived permanently in London, or elsewhere. It was not until the beginning of the nineteenth century that a serious attempt was made to establish the Oxford medical school as a place where instruction could be obtained. This change was due to the exertions of Dr. Charles Bridle Daubeny, professor of botany, and Dr. James Adey Ogle, at that time the Litchfield professor of clinical medicine. These men really taught their subjects, and under their guidance an important advance was made.

But although the professors may have had a great desire to improve the teaching of medicine at Oxford, the regulations in force at the university during the eighteenth century were little calculated to help them in their laudable endeavours. Until 1780 the Regius professor of physic was solely responsible for the instruction in medicine. He was required by statute to give four lectures on the subject of anatomy in the Lent term, and three in the Michaelmas term, but attendance upon these lectures was not obligatory on the part of the students. He was not called upon to give any lectures in medicine, and until the foundation of the Litchfield professorships in 1780 no instruction in that subject was given.

The number of students attending the professor's lectures in any one term rarely exceeded five or six, although many more were in residence. Even the professor's lectures on anatomy could not have been given with any prospect of success but for the fact that generally his lectures were regarded as fulfilling the terms of the Mathew Lee lectureship in Anatomy at Christ Church. The university possessed no dissecting room or museum, and when the professor was fortunate enough to obtain a subject, it was at the dissecting room in Christ Church that the dissection took place. Although Lee founded his lecture for the benefit of six students from Westminster in residence at Christ Church, those students were not obliged to attend, and eventually the lectures were thrown open to all in the university. The same conditions obtained with regard to the Litchfield and Aldrich foundations, and so late as 1834 Dr. John Kidd told the Parliamentary Committee that the professors had frequently advertised their lectures, but had been unable to deliver them on account of the lack of students. Botany was in a somewhat different position. As long ago as 1669 a chair had been established, and a fair attendance of students was secured, more because the subject was regarded as forming part of a polite education than as a serious study. In the circumstances narrated above the Oxford medical school displayed hardly any activity, and it became the chief duty of the Regius professor to preside in the schools over the acts and exercises required for the medical degrees. The exact method of keeping these acts must now be investigated.

The regulations governing the acts and exercises prescribed for medical degrees were formulated soon after the beginning of the seventeenth century, and remained in force until 1781. Under these regulations no one could proceed to the degree of Bachelor of Medicine until he had become successively a Bachelor and Master of Arts, and after taking the latter degree a period of three years had to elapse before proceeding to the M.B. degree. Since it took seven years to become a Master of Arts, the degree of Bachelor of Medicine could not, therefore, be taken until ten years after entering the university. Four years more were required to elapse before the degree of M.D. could be taken, and thus the whole curriculum embraced a period of fourteen years, of which seven were supposed to

be spent in medical study. After 1781 the statutes were amended in such a manner that the three years between the M.A. and the M.B. degrees were contracted to one year, and the four years between the M.B. and M.D. degrees, to three years. In this way the complete curriculum occupied eleven years instead of fourteen, and the medical part of it four years. After taking the M.A. degree, and often after the B.A. degree, the medical student left the university, and nothing more was heard of him until he presented himself for the degree of M.B. No doubt he applied himself with more or less diligence to the study of medicine at some school, either in the British Isles, or on the Continent, but it does not appear that any certificates of having studied physics were ever required by the Regius professor. Indeed, Dr. Kidd, in his evidence before the Parliamentary Committee, distinctly states that no evidence of having studied medicine was required except the word of the individual and the "knowledge of the professor concerning his habits, derivable from the professor's extensive acquaintance." It is true that the professor held the right to examine the candidate if he had any doubt concerning his medical ability, but Dr. Kidd stated that such a course was hardly ever followed. No examination of any kind was required, and on this slender evidence of medical knowledge, the professor gave his certificate to the university which entitled the candidate to the degree of Bachelor of Medicine, after keeping two merely formal acts.

The "Acts" or medical exercises for the M.B. degree, were kept in the following manner. Two questions, previously approved by the professor, were disputed by the candidate on two separate days; on one day the candidate acted as a respondent, and on the other as an opponent, the professor of medicine "sitting over him," as the term was, while the disputations were going on. These exercises were merely *pro forma*, the professor never asked any questions, and sometimes the bedel provided the theses. After these acts had been performed, the candidate took the M.B. degree, but this did not entitle him to practise his profession. Before he could do that, he was obliged to obtain from the university a licence to practise, and this was granted on the certificates of the Regius professor and another resident Doctor of Medicine.

The exercises for the M.D. degree, although quite as formal as

those for the M.B., were performed in a different manner. The candidate was required to read six "lectiones" in the public schools. The Regius professor did not attend upon these occasions, on the ground, stated by Professor Kidd, that "the candidate is supposed to be giving information to others." The only person present at this function besides the candidate was the bedel, and he, not infrequently, provided the "lectiones," which might consist of passages from any medical book chosen entirely at the discretion of the candidate. When a candidate applied for incorporation on a medical degree obtained from another university, the procedure was much the same. The Regius professor required of the candidate evidence that he had graduated in arts, and that he was of the same standing from his matriculation as he would have been had he been at Oxford, but no evidence of medical study was demanded. Having satisfied the professor in these respects, the candidate then matriculated at some college, and the following day proceeded to the schools, where he read his "lectiones" in the manner described above. On the same day, or the day following, the degree was conferred, and the whole proceeding did not detain the candidate in Oxford for more than twenty-four hours.

In the above account, which is based on the evidence given by Dr. John Kidd, the Regius professor, before the Parliamentary Committee on Medical Education in 1834, the perfunctory method of conferring medical degrees at Oxford is evident. It must not be thought, however, that Oxford was singular in this respect, for the evidence of Dr. Haviland before the same Committee with regard to Cambridge discloses equal laxness. Nor must it be supposed that the university had always followed this easy-going method, for there is abundant evidence that, in the early days of medicine at Oxford, students were obliged to submit themselves to examinations in order to test their progress. But when students left Oxford and pursued their medical studies elsewhere, the necessity for holding periodic examinations no longer existed, and the formal "act" previous to taking a medical degree was alone retained. The Oxford medical school was, therefore, at its lowest point of efficiency in the eighteenth century, but a reformation was close at hand, and early in the next century the exertions of Ogle and Daubeny produced a salutary change. In 1835 written examinations were

again introduced, and the old perfunctory methods were swept away. Since then the Oxford Medical School has continued to grow and to expand into a large scientific department where the subjects of anatomy, chemistry, botany, and physiology are thoroughly taught. Students after having obtained a knowledge of these subjects still forsake Oxford in their quest for purely medical instruction, but now, when they return for the degree, they have first to pass a comprehensive examination which is a real test of medical efficiency.

ANTONIUS MUSA: HIS PRACTICE AND PATIENTS

By Raymond Crawfurd, M.D. (Oxon), F.R.C.P. (Lond.)

HE who would reconstitute the personality of Antonius Musa takes up the pursuit of a very elusive phantom. A few scattered allusions in the works of the great writers of Imperial Rome, two slender treatises alleged to be from the physician's own hand—these are all the materials for the task.

A Greekling, as were nearly all his medical *confrères* in Rome, we know nothing of his family beyond the name of his brother Euphorbus, a physician like himself. Pliny says that King Juba named the spurge plant Euphorbia after him, and that the two brothers introduced the practice of douching the body with cold water after the hot bath, so as to brace the system—a very practical measure of rational hygiene. Thereafter the practice seems to have established itself as an abiding feature of the ritual of balneology in Rome, and Celsus cites it with approbation.

In 22 B.C. Musa springs full-fledged into fame with the rescue of Augustus from an illness that seemed to threaten his life. Pliny and Suetonius Tranquillus give different accounts of the measures adopted by Musa. Pliny says that Augustus was saved by the skill of his physician Musa, who counselled him to eat lettuces, in direct opposition to the advice of his former physician Caius Æmilius. Pliny maintains that, over and above its cool, refreshing properties as an article of diet, lettuce promotes appetite and relieves the stomach of distaste for food, while exercising a remoter effect of making blood. The Romans regarded its therapeutic efficacy so highly that they preserved it in oxymel for winter use. It is difficult even to conjecture what the emperor's ailment may have been, unless perhaps it was obstinate constipation.

Suetonius Tranquillus, however, says that, when Augustus was reduced to a dangerous state by a severe catarrh of the liver that derived no benefit from the hot fomentations ordered by Æmilius,

Musa decided to face the risk involved in reversing the treatment, and cured him with cold fomentations. If, as appears to be the case, the two accounts refer to one and the same illness, we must conclude that both measures were employed by Musa on this occasion. The success of the treatment seems to have dealt a severe blow to the popularity of the warm sulphur springs of Baiæ, hitherto the favourite resort of the Roman valetudinarian. In the 15th Epistle of the First Book, which was written very shortly after the illness of Augustus, Horace writes that

"the village, Baiæ, mourns aloud to see its myrtle groves deserted, and the sulphur springs, that are said to dispel lingering disorder from the nerves, despised, and is wroth with the sick folk who have the courage to place the head and stomach beneath the fountains of Elusium, and seek Gabii and cold country resorts."

Sane murteta relinqui
Dictaque cessantem nervis elidere morbum
Sulphura contemni vicus gemit, invidus ægris,
Qui caput et stomachum supponere fontibus audent
Clusinis, Gabiosque petunt et frigida rura.

Horace tells us that Musa had recommended the same régime to himself, and in somewhat unwonted obedience to his physician he tried first Gabii, 12 miles from Rome, and then Clusium, 100 miles to the north. But Musa was destined not to repeat his success in the person of the capricious Horace, who found these places too cold in winter time. Then Horace enquires of his friend Vala as to the climate, accessibility, and social amenities of Velia and Salernum, Lucanian resorts in the neighbourhood of Naples.

Quæ sit hiemps Veliæ, quod cælum, Vala, Salerni,
Quorum hominum regio et qualis via: nam mihi Baias
Musa supervacuas Antonius et tamen illis
Me facit invisum, gelida cum perluor unda
Per medium frigus.

Augustus rewarded Musa for his successful treatment of himself with a large fee and a gold ring, and erected a statue to him at the public expense side by side with that of Æsculapius.

Pliny refers by name to Musa in one other passage in which he

bears testimony to the readiness with which he cured intractable chronic ulcers with a diet of vipers.

Scribonius Largus, physician to the Emperor Tiberius and author of the famous "De Compositione Medicamentorum,"[1] ascribes the composition of Hiera Picra to Musa. It is impossible now to trace the pedigree of our Hiccory Piccory over its two thousand years of existence. It seems, however, to derive from the Hiera Simplex of Galen, which in turn was a modification of that of Archigenes. Time after time the bend-sinister figures in the family tree and adds to the confusion, for other physicians, notably Rufus of Ephesus and Alexander of Tralles, parented other modifications that have merged in the common stem. We may safely say that the idea of a compound aloetic remedy had taken practical shape prior to the time of Musa, for his elder contemporary Themison of Laodicea had published a definite formula, and it is far from improbable that there may be truth in the popular tradition that it originated among the priesthood of Asclepius in Greece.

Pliny says that Musa in his practice discarded much of the medical theory of the school of which Asclepiades and his pupil Themison were the leading representatives. Asclepiades had linked the rational therapeutics of Hippocrates to a pernicious theory, based on the atomic doctrine of Democritus, of constriction and relaxation of the solid particles of the body. Holding this purely mechanical conception of disease, Asclepiades necessarily laid but little stress on internal medication, and here Musa, as we shall see in studying his treatises, joined issue with him and combated his practice. The two men, however, had much in common, for each adhered in the main to the Hippocratic teaching. Asclepiades sought to implant his own theories on it. Musa, versatile eclectic that he was, with a strong dash of the charlatan to boot, was ready to leave theories alone, and sought rather to accommodate his practice to the inclinations of his patients, and to impress them with the boldness of his innovations.

We pass now to the two short treatises in which tradition has it that Antonius Musa himself speaks to posterity. The first of these, the little tractate "De Herba Vetonica," is dedicated to Marcus Vipsanius Agrippa, one of his many distinguished patients,

[1] Comp. 110.

so that he may always have at hand a souvenir of him. It must be said at once that the attribution of the "De Herba Vetonica" to Antonius Musa is open to the gravest doubt. It is true that the words of dedication to Marcus Agrippa survive, but there is no evidence that these were from the pen of Musa. In structure and substance the treatise has much in common with the "De Plantagine," ascribed to one Lucius Apuleius Platonicus, who has been assigned to the time of Hadrian and Antoninus Pius, and this is probably the reason why the two treatises have been grouped together in some early editions, as though they may have come from the same hand. This, however, merely deepens the difficulty, for a critical study of the "De Plantagine" can hardly fail to suggest that it also belongs to a period several centuries later. The question has only a minor bearing on the main subject of this paper, for I purpose to show how little we learn from the treatise of its author, whoever he may have been. So far as it is possible to judge, the plant seems to be the *Betonica Alepocurus*, or fox-tail Betony of Linnæus. Musa descants on the singular medicinal virtues of the plant: its taste, he says, is not bitter like aloes and absinthe, the good effects of which are handicapped by their nastiness, but patients take it readily, as its smell is pleasant: the mild griping that it produces is a positive luxury. But its unassailable claim is that it is a remedy for no less than forty-seven diseases, of which Musa cites the following:

1. For broken heads.
2. For painful eyes.
3. For headache.
4. For dimness of vision.
5. For watering eyes.
6. For epistaxis.
7. For toothache.
8. For ulcers of the lungs, shortness of breath, and pain in the chest.
9. For consumptives and those who spit up pus.
10. For stomach ache.
11. For hepatic pain.
12. For splenic disorders.
13. For kidney trouble.
14. For pain in the side.
15. For lumbar pain.
16. For belly ache.
17. As a purgative.
18. For the bowels.
19. For cough.
20, 21, 22. For quotidian, tertian, and quartan fevers.
23. For pain in the bladder.
24. For stone.
25. For dropsy.
26. For women in labour.

27. For paralysis.
28. For shivering.
29. For women troubled with coldness of womb.
30. For spitting of blood and pus.
31. To prevent drunkenness.
32. For those thrown out of vehicles.
33. For jaundice or morbus regius.
34. For carbuncle.
35. For bad colds.
36. For tired travellers.
37. For those who are off their food.
38. As an aid to digestion.
39. For those who cannot keep their food down.
40. For pain and swelling of the penis.
41. For those who have taken poison.
42. For serpent's bites.
43. For bites of mad dogs.
44. For fistula.
45. For lumbar pain (cf. 15).
46. For deficient menses.
47. For gout.

Such are the properties that Musa attributes to Herba Vetonica, and he gives appropriate instructions for its employment in each of the morbid states. Further he directs that it should be gathered in August and dried along with its seeds and roots, and then ground to a powder ready for use. Physicians, he says, are aware of the usefulness of the drug, but have no notion of the extent of its usefulness. It cannot be said that we learn much to enhance the reputation of Musa from his dissertation on this drug, which bespeaks a blind credulity in the therapeutic efficacy of a relatively inert vegetable remedy. So far as concerns Agrippa the sting seems to be in the tail, for the forty-seventh disease, gout, was his own peculiar enemy, and we catch a glimpse of Musa in attendance on him during an attack from a story told by Pliny. In the later years of his short life Agrippa was a martyr to gout, and so excruciating was the pain in one attack that Musa, all unbeknown to Augustus, had the courage to immerse his favourite's legs in a bath of hot vinegar. This must indeed have called for more than ordinary courage in both patient and physician: indeed Pliny says that Musa ran the risk of inducing complete motor and sensory paralysis of the legs. Agrippa was not a subject for medical men to play pranks upon: from his birth he laboured under one grievous disability, for, as Pliny tells us, he made his entry into this world of sorrows, contrary to nature, as a foot presentation. Pliny boldly asserts that such children are called "Agrippa," because they are born with difficulty—*ægre parti*. These children of monstrous birth are as

assuredly foredoomed to trouble as the sparks fly upward. At first sight it might seem that Agrippa with all his worldly success was an exception to this natural law, but when we look into his private life and see all the domestic misery afforded him by the adulteries of his wife Julia, the fact that his daughter Agrippina laid a curse on Rome by giving birth to Nero, and that Agrippa himself died at the early age of fifty, we see how inexorable Nature is to those that flout her. If other testimony were needed to this essential verity, we have it in the person of Nero, who also was a foot presentation. Musa seems to have had the knack of turning the tastes of his rich patients to the service of medicine, a valuable faculty to possess. Agrippa revelled in gigantic architectural enterprises: he constructed the great aqueduct still to be seen at Nismes, and the Pantheon at Rome, and just a year after the famous cure of Augustus by the skilled hydrotherapy of Musa he built the first of the great public Thermæ at Rome, decorated it lavishly within and without with paintings, marbles, and statuary. It seems legitimate to infer that in the case of the Thermæ at any rate Agrippa acted under the inspiration of his physician.

The second surviving treatise by Antonius Musa is a booklet dedicated to Mæcenas on the maintenance of health and the prevention and cure of disease. If we are to forestall disease, he says, we must know not only what are the physical evidences of a state of health, but also what are the initial symptoms of disease according to the part of the body in which it originates. Musa takes the appearance of the urine as affording a simple criterion of a state of health. He tells Mæcenas that healthy subjects pass colourless urine the first thing in the morning, reddish before the midday meal, clear again after it, and pinkish before supper. These alternations of appearance are normal, and so long as digestion is unimpaired, the urine should not be turbid. Exercise is apt to deepen the colour of the urine, but if the colour of that passed the first thing in the morning is altered it shows things are amiss. If the health and happiness of Mæcenas depended on his observing this regular alternation of changes in his urine, we can understand why Horace asks him

Cur me querelis exanimas tuis? [2]

[2] Odes II. 17.

Such crude urinoscopy as this falls far short of the precision and particularity of the dicta of Hippocrates in the same field of observation, but we must not forget that Musa is addressing an uninstructed layman, Hippocrates the whole profession of medicine. From this point of departure Musa then passes on to the second part of his thesis, the differentiation of the symptoms of disease according to the seat of origin. Disease, he says, may originate in head, chest, belly, or bladder respectively, and it is essential to know the symptoms peculiar to each.

The symptoms that Musa attributes to disease commencing in the *head* strongly resemble the phenomena of a common cold: headache, frontal heaviness, throbbing of the temples, buzzing in the ears, watering of the eyes, and loss of the sense of smell. Then remedies to purge the head should be held in the mouth, and the head must be kept warm so as to encourage the flow of mucus. If this be not done, humours in the eyes, earache, toothache, and painful swelling of glands are apt to occur, with catarrh and heaviness in the head and even ulceration, so that the hair may fall out. It is interesting to recall that it was imputed to Mæcenas for effeminacy that he would appear in public with his head swathed: his frailty may have consisted in nothing worse than obedience to his medical man.

The symptoms of disease commencing in the *chest* are very suggestive of a cold on the chest. The head breaks out into a sweat, the tongue is loaded, the breath sour, the tonsils sore; there is tossing at night and sleeplessness, weariness of mind, heaviness of the body and itching, trembling of arms and hands, and sudden onset of a dry cough. In the face of such warnings emetics are the remedies to employ, for bile is the parent of all diseases: it is best to get rid of it while fasting, but failing this, vomiting should be induced when the stomach is empty, or after a meal, or while at the bath. It is advisable that those who are apt to need emetics to relieve an overloaded stomach should forestall trouble by fasting every tenth day, for emetics often upset the stomach.

The symptoms of disease commencing in the *belly* are closely akin to what is colloquially described as "having a liver." The belly is upset and may ache; food and drink are distasteful; the knees give way; there is a dragging sensation between the shoulder-

blades, and the kidneys are sluggish; the whole body is oppressed, the feet slow and the legs heavy, and there may be an access of fever. In this condition abstinence is of prime importance, so that afterwards the bowels may be more easily purged, and the heaviness of the body relieved. In severe cases a second day of abstinence should be observed, or, if the strength does not admit of that, only the lightest food, such as a raw egg, should be allowed. Neglect of these precautions leads to disturbance of the bowels, gripes, or trouble and epistaxis.

The symptoms of disease commencing in the *bladder* are a medley common to many diseases and peculiar to none, but vaguely reminiscent of alcoholic gastritis and cirrhosis of the liver. Sufferers after this sort quickly experience repletion; their bellies are distended and rumble; their whole body is depressed, they are apt to yawn and to sleep heavily, and they lose flesh; the urine is dark-coloured and scanty; the genitals may swell, and even calculi are liable to be formed. Musa specifies the internal remedies that should be taken to rectify these troubles, and then proceeds to describe the evil consequences that attend their failure. Then they become dropsical, or suffer with their liver or kidneys, or get pain in the bladder; or become liable to stone and get strangury and swelling of the belly. Musa is clearly convinced that as these troubles commence in the urinary system, so the first essential in treatment is to restore the normal appearance of the urine. But he is willing also to entertain certain subsidiary considerations. For example, the sick man must keep an eye on his strength, both to enable him to support the medicines and to ward off fever and indigestion. Musa names two remedies for this purpose, and adds that they are the two most certain remedies against every disease. The first is abstinence every tenth day from food and drink, followed the next day by bathing and resumption of food. The second is the taking of a health-giving draught, with which for several years he had kept the Emperor Augustus from all ill-health. Here, then, we have the kernel of Musa's system: periodic abstinence, coupled with the regulated employment of the bath, and the internal use of a medicinal panacea. Obedience to lunar influences is enjoined in the directions he gives as to gathering the constituent herbs at the proper season of the moon; for all things, says Musa, as well as the sea and the

brain of man, wax and wane with it. Certain general principles of regimen in matters of food, exercise, and sexual intercourse are laid down, as appropriate to the four seasons of the year.

The little book concludes on a note of altruism, that rings strange in modern ears. "Itaque me tecum habebis, libellum meum legendo": "If you keep my book by you, it will be as good as myself." Modern medical literature is apt to be rather a reminder than a *memento.*

So much and so little do we learn of Musa from a study of his own writings, but above and beyond this a fascination fastens on the man, as we picture him in the circle of as distinguished a company of patients as has ever solicited the care of a single physician. Augustus, Virgil, Horace, Mæcenas, Marcus Agrippa: these are the major constellations of his professional firmament. Musa, and Asclepiades before him, are standing refutations of the belief that medicine was held in contempt in Imperial Rome. It is true that medical practice of the better class was almost exclusively in the hands of Greek physicians, but that was due to the fact that indigenous Roman medicine had never outgrown the limitations of a primitive herbalism, while Greek medicine had developed rationally under the quickening influence of the Hippocratic method. But these Greeks for the most part enjoyed the privilege of Roman citizenship and the social intercourse of the highest in the state, and amassed fortunes from the enormous fees that were ungrudgingly lavished upon them. It was the evil reputation of the lower grades of the medical profession, which are sure to luxuriate where the practice of medicine is unregulated by law, that brought medicine into disrepute in Rome.

Antonius Musa enjoyed the full favour of Mæcenas, and it was to him that Musa dedicated his little book on the maintenance of health. It would be out of place here to enlarge on the social features of the salon of this great patron of all the arts in his house on the Esquiline, to which all the virtuosos of Rome were welcome, subject to the single condition of unswerving loyalty to the Emperor. There stood the great house, high and healthful, surrounded by a splendid garden, and there the Emperor once sought haven in sickness, because it afforded more spacious comfort than his own palace. Mæcenas himself was a man of uncertain health, who must have

taxed the resourcefulness of Musa to the full. Seneca says that he tried in vain by means of distant music to relieve a bout of insomnia, which according to Pliny persisted without relief for the last three years of his life. Whether this was under direction of Musa we do not know, but this we may say, that it would have been in harmony with Greek tradition. Horace has him in mind when he writes,

> non avium citharæque cantus
> Somnum reducent.

The sound of running water failed, too, to give relief; this we know from Horace was a recognized practice of contemporary medicine.

> Labuntur altis interim ripis aquæ,
> Queruntur in silvis aves,
> Fortesque lymphis obstrepunt manantibus,
> Somnos quod invitet leves.

Now, as then, the midnight plash of the neighbouring brook and the song of the waking bird at dawn steal like a soothing balm over the town-weary and sleepless brain. Yet Horace seems half ashamed of these new-fangled notions, and would fain revert to the good old-fashioned Roman way of courting sleep by swimming thrice across the Tiber:

> Ter uncti
> Trasnanto Tiberim, somno quibus est opus alto.

The insomnia of Mæcenas in advancing age was probably referable to arterio-sclerosis: its very intractability goes far to justify the assumption. He had lived a full life in the fullest degree, and maybe had aged his arteries thereby. He was fond, too, of the table and fastidious as to food and drink, and Seneca suggests that his ill-health was due to his self-indulgence, aggravated by the domestic affliction of an unfaithful wife.

Pliny and Varro both assert that Mæcenas suffered with fever all his life, as goats were said to do. Perhaps Horace also has this circumstance in mind, when he writes:

> Non domus et fundus, non æris acerbus et auri
> Ægroto domini deduxit corpore febres,
> Non animo curas.[3]

[3] Epistles I. 2. 47.

We do not know on what evidence their statement was based, and in the absence of thermometry we may go so far as to say that no criterion existed by which it would have been possible to gauge such daily oscillations of temperature as would have been compatible with the busy life Mæcenas led. Still the allusion to the continuous fever of goats must needs set one speculating as to whether Varro and Pliny had stumbled inadvertently on the track of the micrococcus melitensis. Varro, quoting Archelaus, says, "Capras sanas sanus nemo promittit: numquam enim sine febri sunt":[4] "No one in his senses speaks of a goat as healthy, for they are never without fever"; and Varro also says that it is very difficult to keep goats healthy when they are herded in large flocks, which reads like a communicable infection. Horrocks and Kennedy in the Report of the Mediterranean Fever Commission state that a febrile reaction has not been observed in infected goats, though some may lose flesh, become poor in the coat, and suffer from a short hacking cough. Pliny, who probably derives his information from Varro, says that, "Goats are never entirely free from fever, from which circumstance it is, probably, that they are more animated than sheep, more ardent, and have stronger sexual passions." On the whole it seems most probable that popular fancy inferred the existence of continuous fever in goats from such characteristic features as those which Pliny specifies as its results: the gestation period of the goat, which is considerably shorter than that of the sheep, the greater frequency of impregnation, and the larger number of young at a birth may have also weighed in the scale. Virgil, who had learnt the ways of goats on his father's farm, speaks more than once of their destructiveness: he depicts the vineyards ruined by them, as though a flame had scorched them, and in another passage he speaks of the caustic poison of their bite.[5]

At the house of Mæcenas Musa will have often met another distinguished patient, Virgil. Suetonius depicts him as a tall man with a big frame, of dark complexion and fresh colour, but withal of uncertain health. He was very subject to dyspepsia, which made him abstemious in food and drink; he suffered from headaches, had a weak throat, and frequently brought up blood. These symptoms, dyspepsia and all, suggest that he was a victim of pulmonary

[4] De Re Rustica II. 3.

[5] Georgics II. 196, and II. 375.

tuberculosis, and there would seem to be confirmation of this in the record of his family, for his brother Silo died while a boy, and his other brother Flaccus in early manhood. His father, who died soon after Virgil reached manhood, had some affection of his eye, which may or may not have been tubercular: his mother, too, seems to have died early. There is a story of Virgil's birth so redolent of medical folk-lore as to justify its mention here. The day before his birth his mother dreamt that she brought forth a laurel bough, which, as soon as it touched the ground, grew into a tree loaded with fruit and flowers; next day, during a country walk with her husband, the child was born in a ditch beside the foot-path. But for all this he was born under a lucky horoscope, for he uttered no cry at his birth. According to local custom a poplar branch was planted at the place, which grew so rapidly that it soon outstripped the neighbouring poplar trees, and on that account the poplar became sacred to Virgil, and an object of devotion to women in pregnancy and parturition. Juvenal alludes to the quickening effect of contact of a fruitful bough, and in one form or another the belief is very widely held.

Suetonius says that among his youthful studies in Rome Virgil included medicine and astrology. His medical studies have left but little trace in his poetry, but for all that perhaps we owe the Æneid to them, for Virgil received his introduction to Mæcenas from that man's chief groom, who was indebted to him for many hints as to the care and treatment of horses and dogs. It is difficult to think of Virgil as an exponent of veterinary medicine, but in his father's homestead at Mantua he must have imbibed as a boy much of the medical lore of the farmyard. The excellent knowledge of field botany displayed in the Eclogues and Georgics would have gone far towards putting him on the path of practical medicine, at a time when herbs formed so large a part of the medical man's armamentarium.

Virgil died at Brundisium at the age of fifty-one, on his way home from a journey to Greece. His death has been attributed to a heat-stroke acquired at Megara, but we know that before starting he felt himself hard pressed by some mortal disease from the instructions he gave to Varius as to burning the Æneid in the event of his death.

Virgil introduced into his Catalecta several lines in praise of Musa, the general sentiment of which is crystallized in the line:

Doctior, o quis te, Musa, fuisse potest.

Tradition has it that in the twelfth book of the Æneid Virgil depicts the character of Antonius Musa in the personality of Iapis. This thesis has been elaborated by Atterbury, quondam Bishop of Rochester, in a dissertation written by him during his banishment from England and published in 1740, after his death, from a manuscript found among his papers. His contention is that, as Virgil in his poems represents his chief friends in the guise of assumed characters, it is not unreasonable to suppose that Iapis conceals the personality of some actual physician; and if so, who so likely as Antonius Musa, physician to the Imperial Æneas as well as to himself? The awkward interpolation of the wounding of Æneas as an elaborate aside, just when the poem calls for unbroken onward movement, for the conflict is in full fray, certainly suggests a purpose outside the immediate current of the story; but, except for this, Atterbury's whole argument is mere special pleading.[6] Still the whole passage of some forty lines is full of interest as conveying Virgil's picture of the good physician. He must choose his calling because he loves it better than all others. He must combine knowledge of the theory of medicine with experience of its practice: it is for him "Scire potestates herbarum usumque medendi." The physician must find favour with God, he must be "Phœbo ante alios dilectus," for in the language of Ecclesiasticus, "of the Most High cometh healing." To Virgil the hand of God is manifest in the miraculous rapidity with which strength returns to Æneas, so that Iapis exclaims: "This comes not by human resource or schooling of art, nor does my hand save thee, Æneas: a higher god is at work." Atterbury concludes very logically that, as you would hope to avail yourself of such adventitious help, so you should be careful in the choice of a physician, that his character is such as is likely to commend itself to the Almighty.

It cannot be said that Atterbury's identification of Musa is established. Now and again Virgil seems to be making contact with some real person, and then all at once he breaks off into con-

[6] Æneid XII. 391–430.

ventional poetic imagery and passages lifted bodily from the Iliad.

It was Virgil who introduced Horace to Mæcenas, and in this circle Horace passed within the professional orbit of Antonius Musa. There is little evidence that he committed the care of his health whole-heartedly to Musa: he is the type of man that plays the wanderer, paying lip-service to many doctors and obeying none: thus while he dubs his doctors faithful, he speaks of them in the plural.[7] We know not a little of Horace from his own poetry. He was very short, dark-skinned and black-haired: towards middle life he grew bald and very fat, "a pig in the sty of Epicurus." Augustus rallied him on his stature very much as Charles II rallied Sir Christopher Wren. As a young man he enjoyed fair health, but even in early manhood his digestion seems to have troubled him. When he was twenty-eight he was suffering from sore eyes and a digestion that demanded respect, for when, on the trip to Brundisium, Mæcenas played tennis, Horace declined the game in favour of a nap, and found that he could not hold his own with his fellow-travellers at table. Dyspepsia was his life-long enemy, and as with many dyspeptics his sufferings were often on his tongue. Maybe Horace had brought some part of his sufferings on himself; like many others who sing the praises of the simple life, he had had his share of the banquets of the great, which he tells us consisted of a profusion of fish, meat, and poultry, with wines of every kind and a supplement of cakes and fruit. When a dyspeptic goes home nightly to a supper of vegetables, leeks, pulse, and fritters, one is not surprised to hear that his belly is at war with him. The diet may be simple, but for a dyspeptic it is simple-minded also. Horace was alive to the fact that no small part of the physical ills of mankind derive from an ill-ordered or ill-occupied mind; yet the manifold allusions throughout his poems to a variety of human ailments bespeak a man whose mind was too much focussed on his body. It is to the credit of Horace that his ill-health did not sensibly affect the temper of his work; just when he was a victim of dyspepsia we find him writing his gayest and lightest odes, having turned his back for ever on the mordant satire of his heady and healthy youth. At the age of fifty-seven he died suddenly of some unknown cause.

[7] Epist. I. VIII. 9.

SOME PERSONAL REMINISCENCES OF SIR WILLIAM OSLER

By J. Beattie Crozier, M.D., LL.D., London

SIR WILLIAM OSLER left Toronto University for McGill in the year 1870, when I entered. We came to London together in 1872 with other Canadian medical graduates to get English degrees. I attended the University College Hospital for the clinical work necessary for the English examination, and when I had passed the College of Physicians I decided to remain in England for my literary work, which was my main object in life, and not to return to Canada like the rest.

I went regularly for years, off and on, to most of the hospitals to pick up clinical knowledge of the various specialisms. Osler, on the other hand, during that time concentrated entirely upon work in the laboratories at University College Hospital under Sharpey, and under Professor Schäfer, now Sir Edward Schäfer, who was then a rising young investigator and has since become a very distinguished physiologist. Then I lost sight of Osler, and we next met casually on Holborn Viaduct sometime about 1874, when he told me he had been in Germany pursuing his pathological studies under Cohnheim, and was going back to Canada. I wished him good luck and we parted. Later I heard from our common friend Professor Wesley Mills that Osler was making his mark at McGill University in pathology, and that it was through Osler's influence that he had himself obtained the Chair in Physiology. Mills told me, I remember, that Osler was the best friend he ever had.

I came across Sir William again in the late eighties, and yet again when he was in London in 1892. This was soon after his marriage, and we had a long talk together at St. James's Hotel, Piccadilly. We discussed the respective advantages of the life of a medical consultant and that of a physician working only in the wards and laboratories of his hospital. He said that the laboratory

and post-mortem room still exercised the greater fascination over him, but he recognised that as things were then there was little future for the pathological researcher.

When next I saw him, some eight or ten years later, I found that the problem had been solved. Firmly established at the Johns Hopkins Hospital, he had secured for himself a position such as no London physician and probably no other British physician possessed. He described to me how he was not only one of the medical staff, with so many beds and wards in his charge, but was the head of an entire Medical Department. By this arrangement he became the general overseer of all the medical work in the hospital, and had access to all cases. I came thus to understand how he had acquired that immense experience in clinical medicine to which his great book on the "Principles and Practice of Medicine" testifies.

I remember an incidental remark that fell in the course of our conversation. He told me that it was quite usual for him in Baltimore to get up in the night to see for himself any post-mortem of obscure and interesting cases that had died in the hospital and had to be examined at short notice, in order that he might personally verify or correct the diagnosis made during life. I no longer wondered why he had made so great a mark as a physician, and understood why medical friends spoke of him as the greatest all-round physician in the English-speaking world.

As for his personal kindness, it was only recently that he burst into my bedroom at half-past eleven in the morning, having heard from someone that I had heart trouble, and said that he had come out specially to see me and examine me for himself. I had not seen him for five years, the last time being at the Athenæum Club, which I have not been able to attend since the opening of the War, owing to my blindness.

All hail, therefore, on your birthday, my old friend, whose celebrity is the greatest and most deserved that Canada has yet produced!

Long life, then, too, and prosperity still, my dearest, oldest, and best of friends!

IATRO-MATHEMATICS

A PLEA FOR A MORE GENERAL APPRECIATION OF THE VALUE OF APPLIED MATHEMATICS AND EXACT QUANTITATIVE METHODS IN BIOLOGICAL SCIENCE

By Georges Dreyer and E. W. Ainley Walker,
Department of Pathology, University of Oxford

Sine mathematica non possunt sciri scientiæ istæ.—Roger Bacon

THE Regius Professor of Medicine in the University of Oxford is accustomed jestingly to speak of the Department of Pathology as a home of modern iatro-mathematics. Many a true word is spoken in jest. Let it be hoped that the aims and aspirations of that department, if not its accomplishment, may cause Sir William Osler's jest to hit the mark. For without exact quantitative methods and the just use of applied mathematics in the interpretation of results medical science, and indeed the whole of biological science, must remain for ever outside the category of exact sciences.

Not until it is admitted that the data of biology are subject to the same laws and susceptible of the same kind of treatment as other scientific data will biological science cease to figure as a kind of Cinderella in the eyes of those who pursue the study of the sciences which alone are at present regarded as exact.

In every age and period the prime duty of the scientific worker is to try to arrive at data and experimental results which represent facts and which record actual observed phenomena in such a manner that their value as observations will always stand, whether the interpretation put upon them at the moment be correct or erroneous. Only in this way can the labour of experimentation and observation be made to produce permanent and indestructible additions to learning, by producing a material reliable and readily available to all future workers. For none can tell whether the conclusions which appear to him indubitable will withstand the test of extended knowledge and new facts. The individual worker and his temporary interpretations pass, but the science remains.

On the mantel of the fireplace in the Regius Professor of Medicine's room at Oxford are carved in golden lettering the words of Hippocrates,

ΒΙΟΣ ΒΡΑΧΥΣ· ΤΕΧΝΗ ΜΑΚΡΗ· ΚΑΙΡΟΣ ΟΞΥΣ· ΠΕΙΡΑ ΣΦΑΛΕΡΗ· ΚΡΙΣΙΣ ΧΑΛΕΠΗ·

"Life is short, art long, opportunity brief, experience dubious, judgment difficult."

There the legend stands beneath the pictures of Linacre, Sydenham, and Harvey, a silent admonition—equally a warning and a stimulus—to every follower of Æsculapius in our Oxford School. No more fitting words could have been chosen by old Sir Henry Acland to form a motto for the restored and rejuvenated School of Medicine. They have stood and ruled throughout the reign of three great Regius Professors of Medicine in Oxford—Acland the courtly scholar, man of tact and learning, who bridged the gap between the old and the new; Burdon Sanderson the thinker and man of inspiration; Osler the great physician, equally at home in the wards, the laboratory, and the post-mortem room, and full of all the learning of the ancients; alike to colleagues and pupils a living, vivifying stimulus. Thus his influence and work bring back to-day the words of Hippocrates with new and living meaning. For short as may be the life of the individual, and brief his opportunity for work, yet his science lives on after him. At every period the interpretation of experiment is dubious, and a true judgment difficult. But real facts gathered in in every generation by each genuine and honest labourer stand for ever as a permanent addition to that edifice of learning that is surely eternal.

Nowhere has the spirit of the true scientific observer been expressed more simply or more modestly than in the words of John Hutchinson early in the nineteenth century in his paper on the Respiratory Functions.

"The matter [he says] of this communication is founded upon a vast number of facts—immutable truths, which are infinitely beyond my comprehension. The deductions, however, which I have ventured to draw therefrom, I wish to advance with modesty, because time, with its mutations, may so unfold science as to crush these deductions, and demonstrate them as unsound.

"Nevertheless, the facts themselves can never alter, nor deviate in their bearing upon respiration—one of the most important functions in the animal economy."

These noble sentences constitute the most admirable text that we have found for what it is now intended to discuss.

The plea that biology can be made an exact science is not so far removed from reality as some would have us believe. Every day an increasing number of its phenomena are rendered capable of exact measurement by the use of properly devised methods. And the idea is clearly not so paradoxical as at first sight it might seem, when one remembers that in *every* branch of natural science the accuracy of observation finally attainable is wholly dependent on the biological function of sight, hearing, touch, or smell. Moreover, even where the physical and chemical methods of measurement or mere detection at present available altogether fail, the biological test often still affords conclusive and sometimes even quantitative evidence; as, for example, in the case of smell and some perfumes, faint light and the dark adapted eye, the detection of certain substances in solution by their fluorescence, or the measurement of some bacterial toxins. Furthermore, the irregularities and discrepancies, often only too easy to point out in biological observations, will usually prove on closer examination not to be haphazard or inexplicable, but to possess some clear and definite meaning, if they are not merely due to faults of method.

One of the first pitfalls which lies in the path of the scientific observer is the danger of endeavouring to compare things which, though at first sight they may appear to be comparable, are not in reality so and sometimes are not even *in pari materia*. Thus, for example, children have always a lower hæmoglobin percentage in their blood than adults, women lower than men. If, then, we mass the material together to arrive at an average hæmoglobin percentage for the human species, we obtain a figure which bears no true relationship to man, woman, or child. For we are not dealing with a sufficiently closely comparable material. Again, if one examine the hæmoglobin percentage of the blood in a hundred normal adult individuals, one finds a certain range of variation. But if one next examines any one of these individuals at different periods or at different times of day, one will also find a similar

variation. We cannot, therefore, conclude that the variations found in the hundred are to be regarded as true individual variations from a mean of the species. Pursuing the problem one step further, one finds that the difficulty of variation in the individual is only partially obviated by the experiment of making each successive observation at precisely the same hour of the day. Put briefly, if we examine him in the mornings we shall find a daily variation in hæmoglobin percentage which is very much greater than that found in observations made in the late afternoon. Accordingly, if we wish to compare different individuals, we must compare them at the hour which we find to be the hour of their own least variability. Only in some such way as this is it possible to arrive at a true estimate of normality.

Moreover, a true determination of normality can be obtained only by taking in large numbers of individuals. Because among subjects which are to all appearance typical healthy individuals of the species concerned there will always be some that are not really normal in the particular direction under investigation, and perhaps some so-called freaks far above or below the line. The irregularities produced by the chance inclusion of such individuals might lead to an entirely false estimate of normality if occurring in a short series of observations, but cancel one another and disappear when the number of individuals examined is sufficiently large.

In many important branches of biological science the discovery of the normal is the sum total of the aim in view. But equally in those branches of science where the object is to discover the cause and character of divergences from the normal, and the conditions under which such divergence occurs, the first essential is a true and accurate determination of the normal. For it is obvious that in the investigation of pathological problems, for example, unless one begins by ascertaining with the most extreme precision attainable at the moment, not only the normal, but also the limits of normal variation, it is a mere absurdity to proceed with the inquiry.

While in ordinary routine it is recognised, for instance, that the size of organs must be judged of in relation to the size of the subject concerned, yet it is still more important to recognise that when one comes to deal with more subtle problems, and requires to penetrate more deeply into such questions as how size is affected by

abnormal conditions, one cannot hope to arrive at true conclusions unless one has first succeeded by the use of proper methods in discovering the possible limits of normality. Here it is only too often found that pathological investigation has to begin with an inquiry into the normal before it can proceed to the study of disease. Spade work has often to be done on purely physiological problems, before the pathological inquiry can be approached or the nature of the problem defined. There is thus an inseparable link between pathology and physiology, similar to that which obliges the astronomer to be a mathematician (though the mathematician need not be an astronomer), or compels the geologist to seek a close acquaintance with some branches of zoology and botany.

To establish facts precisely, in whatever branch of science, the fundamental requisite is accurate and reliable technique. Without good technique good and trustworthy results cannot possibly be obtained. "Die Methode ist Alles" (Ludwig). It is sometimes maintained that problems in biology are so extremely complicated and technique so difficult that approximate results are all that can be hoped for, and that extreme accuracy of measurement is superfluous, and may even be misleading. But we venture to profess the belief that *technical difficulties do not exist save to be overcome*, and that once they are overcome the observer has the gratification of discovering that the phenomena which appeared to be so inharmonious and variable are in reality amazingly regular and harmonious.

To arrive at this result it is first of all essential to make sure that no method is employed until it has been proved by the most careful trial to be *a valid method*. It must be submitted to extended and detailed test and criticism and minute scrutiny from every aspect if its application is to escape the danger of leading into new and unforeseen mistakes, quite apart from mere inaccuracy of observation and personal error. A good illustration of the point which we wish to enforce is the following: In many investigations of different kinds it is desired to remove known quantities of blood from an animal by bleeding. In hundreds of such experiments it has been tacitly assumed that a given quantity of blood removed from a vein by bleeding was actually that quantity of the animal's original blood. But the fact is that this notion is entirely unwar-

ranted. A normal animal submitted to hæmorrhage begins so rapidly to restore lost volume of blood by taking body-fluid into its vascular system, that dilution is continually taking place throughout the bleeding, and can be detected almost from the start. The greater the relative quantity of fluid removed and the slower the rate of bleeding the greater the dilution. It is already marked by the time 5 per cent of the total blood has been removed from the ear vein of a rabbit or from a man by venesection at the bend of the elbow. Accordingly unless the degree of dilution is properly estimated at the time, and the appropriate correction made, the actual quantity of original blood removed can never be known. The whole subsequent investigation, therefore, starts from a false premiss, and the conclusions drawn are inaccurate, and may prove entirely misleading.

Similarly it is a usual practice to employ certain drugs in anæsthetising experimental animals; the experiment then proceeds on the supposition that the anæsthetised animal still possesses its original and normal blood volume. It is the fact, however, that the substance used has frequently produced a marked alteration in the blood volume. Thus chloral hydrate in the ordinary doses used for anæsthesia causes a very definite reduction in blood volume, which entirely alters the conditions of the whole experiment, and this factor is one which possesses great importance and requires close attention in all experiments on the blood and circulation and on respiration, although hitherto it has commonly remained unrecognised.

Again, the attempt originated by Gréhant and Quinquaud to determine the blood volume of animals by administrating known quantities of carbon monoxide in the air breathed affords a striking example of a method which at first appears extremely simple and attractive, but when submitted to critical analysis proves quite fallacious. It is incapable of giving a true measure of the circulating hæmoglobin because the carbon monoxide taken up is divided in unknown proportions between the circulating hæmoglobin and that present in extravascular situations. And this proportion is not constant in animals of different size within a species because the amount of extravascular hæmoglobin increases steadily from youth to adult age. The ratio, whatever it may be, becomes also greatly deranged in many important pathological conditions, e.g.,

blood diseases. The method was therefore wrong in principle for the purposes proposed, and the results which it yielded were necessarily inaccurate.

Points of essential importance in the selection and elaboration of a quantitative method of observation are first and foremost that it must be based on valid principles. It must, so far as practicable, be so devised that the observer can remain in ignorance of the result until his observation is completed, so that in a series of repeated readings he remains unprejudiced by previous results. It must be capable of exact repetition. And its results must aim at expression in absolute numerical values.

Methods have frequently been devised, have been carried into almost universal use, and regarded as extremely accurate, merely on account of their apparent simplicity. An example of this is the method used with various modifications for determining the number of red blood corpuscles in a given volume of blood. The results obtained are accepted as accurate, and one has sometimes found them regarded almost as "gospel truth." But, in fact, few methods exist more studded with pitfalls for unwary feet, or whose results are more generally entirely inaccurate. Among these pitfalls are irregularity of mixing, inequality in cell content of successive drops from the same mixture owing to effects of gravity and of surface tension, and the difficulty of equable and uniform adjustment of the cover-slip upon the drop on successive occasions—to mention only some of the causes of erroneous determinations. Accordingly the results obtained by these methods will be found to present the most astounding variations as soon as the observer submits them to proper controls. Should this sound a hard saying, one can only observe that it can be fully confirmed by any worker who will take five successive drops from the same mixing pipette and compare the five results obtained by counting the same number of squares in each case and always enumerating at least 1000 cells. All these difficulties can, however, be surmounted by the use of suitable procedures.

Next in order comes the recording of one's observations. The experimental data secured must be set forth in such a way that they become a permanent addition to the sum total of knowledge. They must consist of observed facts and not of the observer's interpre-

tations or summaries of facts. Otherwise, should the interpretation be erroneous the whole laboriously collected material is lost or rendered useless. For example, if we say that for a particular drug or toxin such and such a quantity per kilogramme of body-weight is lethal to a given species of animal, without at the same time recording the actual weights of the animals employed and the actual dosage, the data can be of any permanent value only on the assumption that the lethal dose bears a simple ratio to the weight of the body, and that age, sex, and size possess no important influence within a species. But this is not the case. Similarly in relation to blood volume, measurements of volume recorded as percentages of body-weight without corresponding records of the actual body-weights of the animals examined are found to lose their scientific value, when one discovers that blood volume is never in simple proportion to the body-weight, but is a function of the surface area.

Hence in recording data one must, as a minimum, always record those absolute measures on which one's own numerical statements (percentages, etc.) are based, and where practicable it is a most valuable practice to note also such other simple measurements as experience in the past has shown most likely to be of interest and importance, e.g., weight, size, sex, age, and the like.

All science begins in qualitative observation. The gradual evolution and development of an exact science out of what was at first a mere empiricism rests entirely on the introduction of quantitative measurement. By measurement alone can accurate knowledge of the processes of Nature be attained. In the words of Stephen Hales (1727) we may say that:

> "Since we are assured that the all-wise Creator has observed the most exact proportions of number, weight, and measure, in the make of all things, the most likely way to get any insight into the nature of those parts of the creation which come within our observation, must in all reason be to number, weigh, and measure. And we have much encouragement to pursue this method of searching into the nature of things from the great success that has attended any attempts of this kind."

Fundamental as is the importance of the questions thus far dealt with—accurate technique, valid methods, homogeneity of material, and due recording of data—the most difficult and delicate part of

the investigator's work is still to come in the proper handling of the information gathered.

Here he must free his mind from bias, and escape all preconceived ideas. In nearly all investigations some kind of working hypothesis is a natural basis for experimentation, and may be absolutely necessary to give direction to the course of the inquiry. But once the facts have been determined, their interpretation must escape subservience to preformed hypothesis and theory. There is so often a danger that subconsciously the facts may be wrested to fit preconceived theories. It is always so much easier and more tempting to philosophise at large, and build one's facts around an imposing edifice of theory, than to start simply from the sure foundation of the fundamental facts and let the theories grow out of the gradually rising edifice of assured knowledge and accumulative evidence. If one allows one's mind to be unduly obsessed by an attractive theory based purely on speculation, it is so very human to explain discrepant findings as due to experimental error. While if the facts had been approached with an unbiassed mind these same apparently discrepant results might have proved to be the most valuable and valid observations for the development of a truer interpretation.

"A hair perhaps divides the false and true."

And it is the business of the scientific worker to learn from Nature how phenomena proceed, not to teach her how he thinks they ought to proceed.

The dangers inseparable from too great indulgence in the pleasing pastime of pure speculation can be escaped only by accepting no hypothesis which will not stand the test of the most crucial and exacting experiments. Even the master mind of Helmholtz felt this danger of pure speculation, as he lays down so admirably in one of his letters to Ludwig:

"For the time being [he says], I have laid physiological optics and psychology aside. I found that so much philosophising eventually led to a certain demoralisation, and made one's thoughts lax and vague; I must discipline myself awhile by experiment and mathematics, and then come back later to the Theory of Perception."

Experiment and Mathematics were Helmholtz's cure for the ill effect upon the mind of that unrestricted speculation which may so easily destroy a true perspective and disorder scientific judgment. In the application of mathematical analysis to exact data gathered by experimentation lies the whole kernel of the thesis which we wish to advance. This alone can convert the apparently irregular and often merely qualitative observations of natural history into an exact science of biology.

The aim of mathematical analysis is the elucidation of new laws for whose discovery the play of creative scientific imagination is essential, as well as the proper application of statistical method to material which could not otherwise be readily subjected to mathematical treatment. But as Karl Pearson has admirably expressed it:

> "This (the scientific imagination) has to be a *disciplined* one. It has in the first place to appreciate the whole range of facts, which require to be resumed in a single statement; and then when the law is reached . . . it must be tested and criticised by its discoverer in every conceivable way, till he is certain that the imagination has not played him false, and that his law is in real agreement with the whole group of phenomena which it resumes."

In attempting to arrive at an expression in mathematical terms for experimental data it is essential that the range of experimental error should have been ascertained. This alone can enable the investigator to determine whether observations which appear to fall outside his hypothesis are adequate to render that hypothesis untenable, or may be attributed to error of observation. If their deviation exceed what may permissibly be attributed to experimental error, the provisional hypothesis must at once be abandoned. Otherwise we shall easily fall into the tempting quicksand of excluding from our analysis as fallacious those observations which do not happen to agree with our working theory, when in reality they actually provide proof of the erroneous nature of our hypothesis. Only by the inclusion of *all* the data which are not *proved* to arise from experimental errors can the true interpretation of the phenomena be reached.

In applying mathematics and statistical methods to experimental

data it is essential that either the observer himself, or some other worker *fully acquainted* with the subject of investigation and the particular branch of science concerned, shall deal with the material collected. Not even the most complete command of mathematics alone, or even of mathematics supplemented by a knowledge of some other experimental science, will necessarily prove sufficient to prevent a mathematical misinterpretation of data.

For example, if one wished to determine the influence of certain factors on the size of the heart, but began with the fundamental error of supposing that the size of the normal heart was a simple linear function of the body-weight, as has actually happened, no mathematical analysis of the size of abnormal hearts, however carefully and skillfully conducted, could lead to any but erroneous conclusions. Such fundamental misconceptions are only likely to be escaped, or discovered in time when the mathematical analysis of the experimental findings is in the hands of a worker fully conversant with every aspect of the scientific problem and all the details of the experimentation. Hence it is most desirable that *training in the application of mathematics to experimental results should be made an integral part of general scientific education.*

Moreover, before we begin to apply statistical methods we must make absolutely certain that our observations are qualitatively *in pari materia.* For if the material is not strictly commensurable, its statistical analysis will be unavoidably misleading. For example, the statistics bearing on the protection obtained by inoculation against typhoid fever in the South African War appear to have yielded quite equivocal results, perhaps because at that time paratyphoid fevers were not sufficiently distinguished from typhoid fever. Hence among the cases recorded as typhoid fever in inoculated persons there were probably an unknown number of cases which were really paratyphoid fever. But now that the qualitative difference between these infections is adequately recognised, the statistics bearing on the prophylactic use of typhoid and paratyphoid inoculation are found to prove indisputably the great protective value of this measure.

Thus we see that, however simple the problem of the moment may appear, it is always necessary to employ the most careful observation, the most accurate technique available, valid methods,

and correct mathematical analysis, before we can hope to reach a true result. But however carefully we plan, observe, and calculate, there is no sure and royal road to discovery. For as Helmholtz has said:

"The first discovery of hitherto unknown laws of nature, i.e., of new uniformities in the course of apparently disconnected phenomena, is an affair of wit—taking this word in its widest sense—and comes about in nearly every case only by comparison of numerous sensory concepts. The completion and emendation of what has been discovered subsequently devolves on the deductive labour of conceptual and preferably mathematical analysis, since it all turns finally on equality of quantity."

Thus in attempting to bring experimental data under the rule of mathematical law our survey must be so directed as to establish the *right* relationships where relationships are involved. In endeavouring to define new laws we must endeavour to arrive at *rational* formulæ. In a word, we must seek simplicity of expression, because Nature has so continuously shown herself to be simple. We shall then at least have followed the right road. What fortunes meet us by the way, what successes we achieve, what failures strew the path, is matter of less moment.

τᾶυτα θἕων ἐν γούνασι κείται

Not every scientific worker has the happiness to reach the self-appointed goal of his ambition in the discovery and elucidation of new natural laws. But though no worker can command success, all can do more—deserve it!

"So when that Angel of the darker Drink
At last shall find you by the river brink
And, offering his Cup, invite your Soul
Forth to your Lips to quaff—you shall not shrink."

SWEATING SICKNESS IN MODERN TIMES

(SUDOR ANGLICUS, SUEUR DE PICARDIE, SUETTE MILIARE)

By Michael G. Foster, M.D. (Cantab.), F.R.C.P. (Lond.)

Col. A.M.S., Consulting Physician, British Troops in France and Belgium

"Thus what with the war, what with the sweat, what with the gallows, and what with poverty, I am custom shrunk."—*Measure for Measure*, Act I, Sc. ii.

WHEN the army of King Henry VII landed at Pembroke in Wales on 7th August, 1485, to begin their march which ended in the victory of Bosworth Field, a new and hitherto unknown pestilence broke out which rapidly spread over the whole country with extremely fatal results. The features of the malady were sudden invasion, profuse sweating at the onset, which continued for the earlier days, "passion of the heart," and pain in the stomach. This disease reappeared in an epidemic form in 1506, 1517, 1528, and finally in 1551. In 1552 Dr. John Caius, founder of Gonville and Caius College in Cambridge, and President of the Royal College of Physicians, embodied his experience of the epidemic of 1551 in a treatise entitled "A Boke or Conseil against the Disease commonly called 'The Sweate' or 'Sweating Sickness.'" From the study of Caius' book, the dominant features of the disease are, the large number of rapidly fatal cases, or with the knowledge of other plagues, what we should now call "fulminant cases"; in the words of Caius, "some in one hour, it destroyed many in two, and at the longest to them that merrily dined it gave a sorrowful supper." With the epidemic of 1551 the sweating sickness disappeared from our shores. For more than 150 years history is entirely silent as to this disease. In the earlier years of the eighteenth century, small and comparatively localised epidemics made their appearance in Picardy. These epidemics varied markedly in their fatality, in other words in the number of fulminant cases, but in other respects the clinical features present a notable resemblance. This latter epidemic has continued in a smouldering form down to the present century, the last epidemic occurring in 1906. The essential features

of the Picardy sweat are a sudden invasion, profuse sweating being the dominant symptom, headache, and what Caius names "passion of the heart," in the language of our own day "palpitation," præcordial pain, and extreme anxiety, and in the more severe cases a sense of suffocation, with the fear of imminent death. In these latter epidemics, however, a fresh feature was remarked, namely, a miliary rash appearing on the third or fourth day, recurring in crops, and followed by desquamation varying in intensity, but often as notable as that seen after scarlet fever. Catarrhal and pulmonary symptoms are entirely absent, the urine rarely contains albumen.

A family tree is universally admitted to be one of the most assailable things in the world, and the true parentage of the Picardy sweat from the Sudor Anglicus has been assailed with all the ardour which is displayed when any other honour is called out of abeyance. Hecker contests the paternity of the Picardy sweat on the grounds that a whole century and vast national revolutions had intervened. And yet the plague disappeared from Caroline England in the seventeenth century and reappeared in Suffolk in the early years of the twentieth. This author, however, suggests the very reasonable doubt as to the "absence of any transitional forms of any duration which would certainly have occurred had Nature intended gradually to form a miliary fever" out of the English sweating sickness. Here, indeed, is one of the weak links in the chain of ancestry, as even the earlier accounts of the Picardy sweat describe the miliary rash, while the records in Tudor times make no mention of any skin eruption. In our own day we are accustomed to think of a rash as a dominant sign, but when we reflect, measles and scarlet fever were not discriminated until a century after the last sweat, typhus fever remained "gaol-fever" until the days of our grandfathers, with no mention of the mulberry rash, and this was not distinguished from the rose spots of typhoid fever until Sir William Jenner once and for all determined their differences. There is, however, very strong evidence available which goes far to prove the essential identity of the two diseases. The first point which strikes one in reading accounts of epidemics of Picardy sweat is that in its non-fulminant forms the disease breeds singularly true. The symptoms described by Caius, profuse sweating, palpitation, epigastric pain, fear of imminent death, are all described over and over again in the French

descriptions. In the one solitary case the writer has had the good fortune to treat while serving with H. M. Forces in Picardy, all these symptoms were present. Further, it may be argued that in the French epidemics the mortality has frequently been so low that it is difficult to reconcile this mild, though extensive, epidemic with the lethal pestilence of Tudor times. But though later epidemics have shown a low death rate, this has in no measure been invariably the case.

Emerit, in describing the epidemic in the Charentes in 1906, speaks of the extreme fatality attending the epidemics in Poitou in 1840 and l'île d'Oloron in 1880, in which whole families were completely carried off in a few days. The tradition of the terrors of these visitations lingered in popular memory, so that the disease was spoken of with dread by the populace in the Charentes in 1906. Two factors are present—that the symptoms of the disease in succeeding epidemics tally one with another, and present a striking resemblance to the descriptions of the mediæval sweat. As regards the fulminating case, a rapidly fatal infection is likely to present largely identical features, whatever the infecting agent. Arguments, therefore, based upon the clinical aspects of fulminating cases can have but little weight; the essential features of the clinical picture are revealed only in cases of greater length, where the body reacts to the infecting organism. Dr. Hamer, a staunch upholder of Sydenham's epidemic constitution, in whose advocacy he has displayed profound scholarship and rare dialectic skill, refuses to recognise Picardy sweat as the descendant of the sweating sickness. Some of the epidemics he regards as being undoubtedly influenza. Against this view must be set the opinion of the late Dr. Chantemesse, who was President of a Commission which investigated the epidemic in the Charentes on the spot. In a conversation shortly before his lamented death, with the writer, he affirmed emphatically that the miliary sweat definitely bore no resemblance to influenza. This opinion was formed, moreover, at a date when influenza had become a familiar disease.

The Charentes epidemic in forty-five days attacked 6000 persons. When the purely agricultural character of the community is taken into account, this constitutes a very widespread epidemic. Emerit states that the respiratory organs were rarely attacked, and catarrhal

symptoms were notably absent. With our recent and sorrowful experience of this disease, it appears inconceivable that an epidemic of influenza could be unattended by many cases of bronchitis and broncho-pneumonia.

Turning to the clinical aspects, the onset of the malady may be heralded by rigors, headache, general malaise: in some cases vomiting and epistaxis are present; an attack of syncope may be the first symptom. Frequently, however, the profuse sweat is the initial symptom. These sweats occur in paroxysms, the whole body being bathed in perspiration which soaks, not only the bedclothes, but also the mattresses. The sweat has, as a rule, no smell; in some cases it has a musty odour, like the straw of a rat-infested granary. Accompanying the sweat, the patient complains of an intense burning sensation, or a feeling as of air moving in his limbs, a symptom also described in the Tudor epidemics. Beside the distress of the sweating, the patient experiences præcordial pain with a sense of suffocation, and intense distress, sometimes accompanied by a sense of impending death. Epigastric oppression and pain in the right hypochondrium add to his miseries. The temperature rises rapidly to 102° or 103°, but the pulse rate is not, as a rule, markedly accelerated. From the second to the fourth day the rash appears, preceded, as a rule, by a feeling of formication. The rash is two-fold, the exanthem proper and the miliaria. The exanthem is reddish and, as a rule, papular, and in contrast to the red spots are the glistening white miliaria. The rash may be scarlatinaform, or purpuric, or in some cases the miliaria coalesce, forming large bullæ. The rash usually appears first upon the neck and trunk, and thence spreads over the whole body; it is often well marked upon the wrists, forming the miliary bracelet. Papules and miliaria both come out in successive crops, the rash lasting from five to seven days. The eruption on the whole bears a striking resemblance to that of measles. Desquamation follows, and may be merely branny or annular, or in large flakes similar to that of scarlatina. In rapidly fatal cases, a petechial or purpuric rash may appear within a few hours of onset. In the more fatal forms, the patient usually succumbs within the first twenty-four or forty-eight hours from a general septicæmia, or a generalised septicæmia may develop suddenly at a later period. The respiratory organs usually entirely escape. The urine is scanty,

owing to the profuse sweating, but contains no albumen. The attack usually lasts from seven to fourteen days, and though convalescence is slow, there are no serious sequelæ.

From a pathological point of view, practically no progress has been made. Post-mortem examination reveals little but the conditions associated with a general septicæmia. In the Charentes epidemic, examination and culture of the blood and cerebro-spinal fluid yielded negative results; inoculations into rabbits and monkeys were equally sterile. The essential virus of the disease is thus entirely unknown.

The method in which the disease spreads is further a matter largely of speculation. The commission appointed to investigate the epidemic in the Charentes state definitely that they could find no evidence of direct infection by contact from one person to another. They instance a large fair at Romillac, an already infected town, where 200 persons from Angoulême spent the day, and did not import the disease into Angoulême. On the other hand, Dr. Emerit, a local physician, regards the malady as probably spread by contact, instancing the local name, *maladie des foires*, in token of its rapid spread after each of the local fairs. This writer further instances the case of a woman who found herself in his waiting room in company with the relatives of a patient suffering with the disease. She returned to her home eight miles away, developed the disease two days afterwards, and remained the only sufferer in the village. The late Professor Chantemesse enunciated the theory that the disease might be due to field mice, and was conveyed to man through the agency of fleas. Chantemesse was led to this conclusion by remarking that in the houses which had been first attacked the inmates were covered with flea-bites. Further, the locality in which the epidemic originated had suffered a plague of field mice, which had been driven into the villages by floods. Also it was noted that inmates of ground floor rooms and notably those without boarded floors were attacked in far greater numbers than others. A similar observation was made by Scholz in an epidemic in Austria in 1905. The sweat has in all recent visitations been strictly confined to rural districts and is in no sense an urban malady.

Sweating sickness must be regarded not as an extinct disease, but rather as one, epidemics of which occur at comparatively long intervals, and to which no definite cause has yet been assigned.

At the time when the distinguished physician to whose honour this fasciculus is dedicated began to teach medicine, systematic treatises contained brief references to diseases then supposed to be on the verge of becoming extinct. To the literature of these diseases the student of antiquarian tastes could devote himself with the ardour of a pure scholar, untainted by any ulterior fear of the examiner's table. Two notable instances were plague and influenza, and yet men of fifty have lived to see these so-called extinct diseases of their student days a menace to the health of the world. Influenza did not reappear till 1889, since when wave after wave has passed over the whole world, culminating in this last and most deadly visitation from which it is to be hoped we are now emerging. Plague, then supposed to be confined to the highlands of Arabia, has become a serious administrative problem in our Eastern possessions. India owes thousands of deaths annually to plague, and this disease has obtained a temporary foothold in almost every country in the world. Other diseases, too, then supposed to be disappearing, have since assumed menacing proportions. "When the people of these islands once more took up the great tradition" and after the lapse of a century, a British army trod the fields of William the Third and Marlborough, it was again exposed to largely mediæval conditions. A campaign often precludes personal cleanliness for a space of many days, and consequently ensures a verminous condition. A return to mediæval conditions reproduced mediæval diseases, the horrors of German prison camps engendered typhus, till then regarded as a rapidly disappearing disease, scabies became a standing menace owing to the number of men it kept out of the Line. Moreover, a new disease, trench fever, clearly proved to be louse-borne, was a greater cause of disability in the rank and file than any other purely medical affection. But for Sir Almroth Wright's method of inoculation, enteric fever would have become so rife that every Base Hospital would have been a veritable Bloemfontein.

It is interesting to remark that in the very district where Picardy sweat was still a noticeable disease, no epidemic occurred under conditions imposed by warfare. It has been clearly shown that less than a decade before the war a considerable epidemic had occurred in France. Isolated cases have occurred in Picardy

during hostilities without engendering an epidemic, where all other known conditions for the transference of epidemic disease were abundantly present.

We can only conclude that as we know nothing about the essential cause of sweating sickness, and can only surmise its method of spread, it does not spread by ordinary channels. And yet mindful of the past, we should be unwise to regard it as necessarily a disease nearing extinction.

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THE LABORATORY AND THE WARD

By Archibald E. Garrod, London

THERE is something amiss with the mutual relations of pathology and clinical medicine in our English schools. These two branches of medical science, which should be knit together so closely, are tending to drift apart, to the detriment of both.

In some recent writings and speeches we notice a tendency to ascribe almost all advances of medicine to the workers in pathological laboratories, and to represent the members of the clinical branch as merely applying in practice knowledge which has been gained in the laboratories. Thus, in a recent book which presents to general readers, and in a most able and attractive way, the story of the "Spirit and Service of Science," the following passage occurs:

> "In the struggle against diseases, and the discovery of means of stamping them out and preventing their development, we must not look for help to the popular physician, but to the pathological or the clinical laboratory, where scientific research is being carried on, often under harassing conditions, and always with inadequate recompense. The ordinary medical practitioner, like the engineer, makes use of scientific results for the benefit of mankind, but originates little for himself. He is able and practical, good at diagnosis and clever in manipulation, but withal an empiric, wanting in scientific ideals and only very occasionally a contributor to scientific knowledge." [1]

There is no single statement in this passage to which serious exception can be taken, and yet I venture to think that it presents a wholly incorrect picture, and that on account of what it does not say.

We may dismiss such comments as that the work of the average medical practitioner is far more harassing than that of the laboratory worker, and is seldom better remunerated, and turn to more important omissions. Thus the writer makes no mention of that large

[1] "Discovery, or the Spirit and Service of Science," by R. A. Gregory, 1916.

body of physicians and surgeons who form the staffs of hospitals with medical schools, and who have in consequence far the best opportunities of advancing medical knowledge, and who are advancing it every day. Yet, although the passage quoted appears to ignore this class, which has in the past produced such physicians as Harvey, Laennec, Addison, Charcot, and Hughlings Jackson, and such surgeons as Hunter, Lister, Bowman, Paget, and Horsley, in the chapter of which it forms part a glowing tribute is paid to the scientific work of Edward Jenner, Lister, and Simpson, and some other practising medical men. Nor should we gather from it that, through the centuries, practitioners of medicine have contributed very largely to the advancement of those primary sciences upon which medicine rests, and have laid far more than the foundations of physiology and pathology. Until comparatively recent times there were no physiologists save medical men, and until much more recently there were none who made the study of pathology their life's work.

The author quoted is an astronomer and physicist, but a like note is struck by others who are themselves engaged on pathological work, and usually with the most worthy object of convincing the British public that the good of suffering humanity is furthered at least as much by the endowment of pathological laboratories, as by the increase in the number of beds in hospitals. It is upon the voluntary contributions of the benevolent that the erection and maintenance of our hospitals depends, and to the public this idea is a novel one.

It is not easy to carry conviction in face of the widespread prejudice against any branch of science which involves tests or experiments on animals. In the circumstances some degree of overstatement is pardonable and even needful. Where hospitals are maintained out of public funds, and administered by governments or municipalities, far less difficulty is met with in securing the outlay called for by this essential need.

But such statements react upon the minds of those who make them, and exert an influence as little favourable to progress as would the action of one oarsman of a racing pair who called out to the spectators upon the bank that the other was not pulling his weight and that it was he who was making the boat travel.

It is a regrettable fact that some pathologists do acquire a certain disdain of clinical medicine, and of those whom they style "clinicians," as of workers upon a lower plane. The term clinician is a good one, which is needed in our language, but has become tainted by this attitude of mind. It has become, so to speak, a class word, employed only by laboratory workers, just as the term allopath, which is certainly *not* a good one, is used only by the adherents of homœopathy.

The clinical worker naturally adapts to his own uses the advances of science in general. The thermometer which gives him a measure of febrile disturbances, the *x*-rays which bring into view parts hitherto invisible, lend him valuable aid, to quote two examples amongst many. In the same way the pathologist in his laboratory avails himself of the discoveries of the makers of dyes, and the skill of the blowers of glass. It seems hardly necessary to point out that the methods of bedside diagnosis which have been devised by physicians and surgeons to meet their own needs are as strictly scientific as the methods of the laboratory. The task of the clinical worker is to detect, by means of their signs and symptoms, morbid conditions which are inaccessible to direct observation in the living patient, but with which he has become familiar in the post-mortem room. Unless he can make a diagnosis he cannot hope to do more by his treatment than relieve symptoms as they arise.

Percussion and auscultation are purely scientific methods. It is by accurate and careful observation that the physician is guided to the conclusion that a pleural sac contains fluid or that a lung is consolidated, that a cardiac valve is incompetent, or that the heart muscle is damaged by disease.

No more beautiful examples of scientific methods and reasoning can be quoted than those employed by the neurologist in localisation of lesions of the brain and spinal cord, and in gaining insight into their nature. It is true that his conclusions are based upon anatomical and physiological observation, which enable him to carry in his mind a stereoscopic picture of the brain as transparent as the stereoscopic images of the radiographer, but the men who made those observations were, until recently, engaged in the practice of medicine or surgery, and some of them might even have been classed as "popular physicians."

Again, the entire groundwork of our modern knowledge of internal secretions was laid by practising medical men, amongst whom were our own countrymen Addison, Graves, Gull, and Horsley, who gained an insight into the functions of the ductless glands by studying the experiments which nature is always carrying out before the eyes of those who have eyes to see them.

In recent times the methods of clinical examination have increased in complexity from year to year. Where our fathers picked up nuggets from a virgin gold field we are reduced to sifting the sands for grains, and improved methods give us untold advantage in the search. But many of the newer methods are so complicated that they can be carried out only by experts, and in a well-equipped laboratory. Thus there has come into being and has developed, within the memory of men who are not yet advanced in life, the new study of clinical pathology.

The science of bacteriology, which owns as its parent that great genius Pasteur, who was by training a chemist, has altered the whole aspect of medicine, and before the bacteriologist lie open fields of study which are independent of clinical medicine. He is engaged upon the study of the living agents of disease whether vegetable or animal, their life histories, their life outside the human body, and their conditions of growth, as well as their effects upon the organisms which they invade, and the complex phenomena of immunity. The record of his work includes some of the greatest achievements of science, such as the campaigns against malaria and yellow fever which have already rid large tracts of the earth's surface of these scourges, and the preventive inoculations against the fevers of the enteric group. These are triumphs of the laboratory and not of the ward, but it is only fair to add that it was a practising physician who discovered the parasites of malaria, and another who propounded the theory of the mosquito carriers.

Pure pathology will doubtless have many triumphs in the future, and in lending its most cordial support to those who study it mankind in general will only be doing the best for its own interests.

But there is still much work ahead for clinical physicians and surgeons, in the advancement of knowledge as well as in the treatment of the sick, and especially for concerted work in which laboratory and ward workers co-operate as colleagues, and without any

claim to a monopoly of the scientific spirit and method on either side. Whereas pure pathology is to a large extent an independent science, the applied branch, to which we give the name of clinical pathology, is, as that name indicates, a branch of clinical medicine and surgery.

The bacteriologist is tempted to form a mental picture of a day when the methods of bedside diagnosis, upon which clinical workers rely to give them a knowledge, of necessity imperfect, of the morbid processes at work in their patients, will be rendered superfluous; when the laboratory will supply a clear-cut diagnosis, certainty in place of doubt, as indeed it sometimes does, and when treatment will be carried out on nature's own lines, by therapeutic agents supplied from the laboratory, instead of by "drugs of which we know little poured into bodies of which we know less."

But that day is still very far off, and the clinical worker realises that every patient is a law unto himself, that human nature calls for treatment of symptoms as well as of diseases; that laboratory findings are little less fallible than clinical inferences, and that in some cases they actually mislead.

A diagnosis can seldom rest secure upon a single finding; the whole picture, clinical and pathological, needs to be taken into account. Very careful examination of a patient is often necessary before the significance of a leucocytosis can be rightly estimated, and even in cases which fall within its special province the laboratory may afford only negative evidence at a time when action is imperative. If a patient's blood contains malarial parasites we are certain that he has malaria, but it does not follow that his symptoms at the moment are due to that cause, any more than the absence of such parasites at a particular time excludes the malarial origin of the symptoms observed.

Again, a large part of diagnosis is concerned with the detection of the seat of a malady, and such diagnosis rests mainly upon clinical findings, although here again the laboratory may render valuable help.

In a word, the modern clinical worker cannot dispense with the help of the laboratory, nor can the clinical pathologist reach his aims without the aid of the clinical worker. They share between them the essential work and both alike are students of science.

If it were possible to concentrate the whole of the scientific work of medicine in the laboratories, and if clinical studies came to be regarded as unattractive to men of scientific instincts, the results would be deplorable for medical practitioners and patients alike. Even now there are signs of diminished zeal on the part of students to become adept at the purely bedside methods of examination. Unless the whole field of medicine be permeated by the scientific spirit we can look for little progress, and shall return to the conditions in the Middle Ages, in which practitioners merely accepted and applied what was to be learnt by study of the writings of Hippocrates and Galen. Indeed we should be in a worse position, inasmuch as degeneration is a more hopeless state than arrested development.

On the other hand, the practitioner cannot respond to the call of science at every moment. He has to deal not only with sick bodies, but also with that uncertain entity human nature. In the sick room the scientific standpoint must often be pushed on one side. He may feel called upon to refrain, on account of the state of his patient, from an examination which promises results of no small interest and importance; and in some circumstances tact and sympathy avail more than professional skill and acumen. The doctor often has to bear with irrational questionings, and to be patient in face of unreasonable prejudice; to cajole or persuade a patient to a course necessary for his welfare. He must humour in non-essentials but stand firm in essential matters. It is true, no doubt, that numbers of those who enter the medical profession are not fired by scientific zeal, whereas no one is likely to devote himself to pathology who lacks such zeal; and in general practice even those in whom the scientific instinct is strongly developed have but scanty opportunities for its exercise. Most have little time for needful rest and relaxation, and no time for constructive scientific work, yet some produce epoch-making results. Edward Jenner was a country practitioner, and examples might be quoted amongst men now living who have opened up fresh fields of research.

But it is obvious that the main seats of clinical progress must be the wards of hospitals with medical schools. In them the workers enjoy far greater advantages. They learn daily from their own

observations, from their colleagues, and from the students whom they teach; they have opportunities of watching all phases of disease, and all modern methods of examination are at their disposal. The *x*-ray room and the bacteriological and chemical laboratories are at their service, and experts in special branches can be called in when necessary. Their observations are recorded and charted, and they have assistance in their work from house-physicians, clinical clerks, sisters, and nurses.

The modern physician or surgeon is in constant need of information which the laboratory affords, and it is desirable in every way that the work of the clinical laboratory should be closely associated with that of the wards; that the laboratory workers should frequently be in the wards, and the clinical workers in the laboratory.

In England this ideal is seldom realised, and the laboratory work is usually concentrated, with pure pathology, in a pathological building. One reason is that our older hospital buildings offer no space for clinical laboratories attached to groups of wards, but even in hospitals of recent construction no adequate provision is made for them. Even where separate clinical laboratories exist they are for general use, and are not associated with particular cliniques. The result is that, although we require our students to undergo a training in clinical pathology, the materials which they examine are often derived from patients whom they have never seen, and the students who are working in the wards do not follow the laboratory work on their own cases. A collection of slips of paper, with bare records, represents the pathological aspects of any individual case, so far as the physicians, resident officers, and clinical clerks are concerned. This, I maintain, is a thoroughly unsatisfactory state of affairs.

Were the clinical laboratory close at hand, and in union with a particular group of wards, some time would be spent in it at each visit of the physician. Frequent conferences between clinical and laboratory workers would help to solve many difficulties, and would save the latter much unprofitable work. The clinical clerk would make his own blood counts and agglutination tests under supervision, and his results would be checked and in important cases controlled by more experienced workers. In this way the students would obtain and retain a far better grasp of the problems of clinical medicine, and of the various means which contribute to accuracy of

diagnosis. The laboratory worker, for his part, would share in the interest of the problems of the clinique, would suggest and receive suggestions as to lines of investigation, and would find his work far less of a routine. When vaccines are employed he would watch the effects of the administration of the therapeutic agent which he has prepared. To the teacher the gain would be equally great, for he is hampered seriously in his attempt to inculcate the principles and methods of diagnosis and treatment, if much of the evidence upon which he relies is presented to him second hand, upon slips of paper.

Half the business of the teacher of any branch of science is to lead his pupils to observe for themselves and to draw conclusions from what they observe; the mere imparting of information is done as well by a text book. But the text book can only teach on broad lines, whereas each individual patient presents some new facet of disease. Only the living teacher, drawing upon experience which can hardly be committed to writing, can convey these *nuances;* he needs to demonstrate at the bedside those points which admit of demonstration there, and then to proceed to the laboratory and see, with his students, what further evidence is furnished by the microscope, the culture, and the test tube. What is for the good of the student, who is the medical practitioner of the future, and of the teacher upon whose teaching the future standards of his pupils rest, is *a fortiori* for the benefit of the individual patient and of sick mankind.

The tie between chemical pathology and clinical medicine is a closer one than that which links bacteriology to the wards, and they show less tendency to drift apart. The chemical pathologist is concerned less with the actual agents of disease than with the disturbances of the body chemistry which they produce in those who suffer from their invasion, and he is dependent upon the co-operation of clinical workers at every turn. Without such co-operation studies of disorders of human metabolism cannot be carried out. The collection and accurate measurement of excreta is dependent upon the care of the nurses, and a still heavier task is laid upon them when the diet must be regulated and its constituents accurately weighed. Indeed the quality of the work in a clinique in which metabolic problems are studied is largely determined by

the care and keenness of the sisters of the wards, and a failure at any point may vitiate a series of elaborate estimations. Upon the medical officers devolves the task of ensuring the required conditions, as far as is compatible with the interests of the patients, and without such co-operation the work of the chemist is reduced to a mere routine examination of materials submitted to him.

The tie with morbid anatomy is still closer. A course of work in the post-mortem room is required of all students, and nearly all clinical teachers have had a long experience of post-mortem examinations. The science of diagnosis is but a shadowy thing unless the physician has a clear mental picture, based upon personal observation, of the conditions which he seeks to detect in his living patients, and which he teaches his students to detect. It would be a sad blow to clinical medicine amongst us if, as is commonly the case on the Continent, the conduct of autopsies were taken out of the hands of those who aspire to be the clinical teachers of the future, and transferred to those of pure pathologists. The gain to pathology is comparatively slight, the loss to clinical medicine is irreparable.

If, as I have tried to show, the close co-operation of laboratory and ward is of advantage to all who work in each, it is essential to medical research. The time is past when a single man could carry out all the clinical investigations possible with the resources at his command; some of the work must be deputed to experts, although the physician needs to be acquainted with the essence of all the methods employed, if not with their technical details.

Thus co-operation has become necessary for the due investigation of a new or obscure morbid syndrome, for the elucidation of any new problem of clinical medicine. There still remains much work to be done by the concerted efforts of pathologists and clinical workers. Such work is best done by a group of men accustomed to work in concert, just as a football side used to playing together may beat a casual concourse of better players; and clearly such work is best obtained by the organisation of the clinique as a unit which shall include both wards and a clinical laboratory. Under such a scheme the continual intercourse of the workers is secured, and the advantages which are derived from interchange of ideas.

Such a unit must have a controlling head, and as the care of the

patients must be the primary consideration he can be no other than the physician or surgeon responsible for their treatment. It would be no more suitable that a pathologist pure and simple should preside over such a laboratory-ward unit, than that a clinical worker should, in these days, be the head and director of the laboratories which have for their province the study of purely pathological problems. For let it be clearly understood that it is not suggested that pathology, as such, should be under clinical control, but merely those laboratories in which the more elaborate clinical methods are carried out.

This organisation of wards and clinical laboratories under a single head is the essential thing, and the details of structure of the clinique so formed are minor matters. There is not the slightest need to copy slavishly any continental model, nor to arrange the work on any foreign plan. The daily clinical lecture which plays so large a part in the teaching in most continental cliniques is in no way essential, although it may be granted that such demonstrations have value, and that in our schools the clinical lectures might, with advantage, be more frequent and elaborate in illustration. We are all convinced of the great value of the English system of practical bedside teaching of small classes, and of the regular attendance of students in the wards, and would rightly look with disfavour upon any change likely to impair such teaching; but the plan here advocated would make for its improvement, by enabling the student to gain a more thorough grasp of the bearing of clinical methods upon the diagnosis of individual cases.

The unit plan is quite compatible with our system of small cliniques under the physicians and surgeons to the hospitals, but the introduction of professorial cliniques *of the continental type* would involve more sweeping changes. Such a clinique is a much larger unit, in which the staff consists of a professor with a large number of beds under his care, and a group of assistants who for the most part hold office for several years. The assistants are encouraged to do original work in the wards and laboratories, have charge, under the professor, of groups of patients, and take a part in the teaching. The original work which they carry out constitutes one of their chief claims to promotion to other posts.

The ideal professor must be a good teacher, and an investigator, and should possess that hormonic influence which stimulates his

assistants and others to pursue research. He will suggest lines of investigation, and discourage work on lines which end in blind alleys. He will exercise a general supervision of the labours of the clinique, and will ensure to each worker due credit for the researches which he carries out.

In a large clinique much of the bedside teaching of the students must be deputed to the assistants, who are usually men of some experience, and the professor's daily clinical demonstration in the theatre is apt to become the most important teaching event in the clinique. In the smaller universities, on the other hand, the professor takes a larger share of the individual teaching of students.

Whilst I believe that the wholesale substitution of this system for our own would not be to the advantage of medical education in general, I am convinced that the setting up of some cliniques of this kind in London would do much to foster medical research, and would prove of no small advantage to "honours" students.

This aim would best be realised by the establishment of a university hospital, with a limited number of professorial cliniques, at which all university students should attend during some portion of their course, and in which post-graduate research work should meet with every encouragement. Having no school of its own it would not enter into competition with the other teaching hospitals, but its influence would tend to react upon all medical teaching.

The professors would be chosen on account of their special qualifications for such posts, from among the best men to be found in the country, and their assistants should be drawn from all the schools. The training which the assistants would receive would prove an excellent preparation for posts on the staffs of other hospitals.

But even if the desire which prevails at the present time for improvement of our system of medical education and the advancement of research should fail to bring about the adoption of such a scheme, much will be gained if it does result in the realisation of the essential need of a closer union than now exists between the laboratory and the ward.

SOCIAL RECONSTRUCTION AND THE MEDICAL PROFESSION

By Sir Auckland Geddes, London

THE Cornish proverb, "Who will not be steered by the rudder will be taught by the rocks," is a dangerous half truth. For four and a half years the devils who demonstrate the folly of human wisdom have bathed the world in blood to show that a rudder is nothing unless it be controlled by a competent helmsman with accurate charts. In result, Prussia and her allies are learning the dread lesson of the rocks.

It is well for us to study this demonstration. Prussia in the days of her pride loved to proclaim the efficiency of her rudder, and her consequent immunity from the danger of shipwreck. Just so to-day we can read in any paper dissertations upon the superior qualities in virtue of which we have defeated the Central Powers. Those who, knowing the manner of our victory, are not convinced by the arguments of the press, may well pray that it is not written in the Book of Fate that we, too, are to graduate from the hard school of the rocks.

We have all heard and wearied of the "Blond Beast." We have all groaned in spirit at the chorus of admiration raised by the Teutonic supermen to celebrate their own superiority. We have heard, some perhaps have believed, that their superiority was the inevitable outcome of their devotion to Science. I should write SCIENCE. To the world, the word Science denotes the sum of facts accurately known about the universe. To the Prussian, SCIENCE was almost synonymous with Truth, and SCIENCE was not only Prussia's rudder, but Prussia's chart. Now on that chart the Darwinian theory clearly could be marked only as a deep. In reality it is the most dangerous of all the reefs, for it appears to elevate to the dignity of a moral law a generalization based on observation of the processes of organic evolution and the elimination of the physically unfit, and from these draws deductions which

are manifestly open to doubt. Applied to human conduct, it places each in antagonism to all, thus crowning self. This violates one of the most profound emotions of mankind, and denies the dearest instinct of the human race.

Science, dealing with the material universe and misunderstood to be dealing with the universe, misled not only the Prussian, but also many individuals in all nations. Science can be materialistic only, but the whole of history shows that in the human control of affairs there is something greater than materialism, and that is emotion. Emotions connected with the ideas of God, of Motherland, of Freedom, drive, as they have always driven, millions to die gladly to testify to the faith that is in them, and emotions have complex relations to accurate knowledge. They may spring from Science. They may feed on Science. They may be killed by Science, but never yet have they been steered by Science. Science, in fact, is not of the stuff from which human rudders can be made. Science can help to plot the charts. Science can help to train the helmsman, but never until Science and Truth are synonyms can Science steer.

During the short span of our generation physical and biological science have killed the emotions of religion and the Christian ethic in the minds of millions. Simultaneously medical science has helped to generate an emotion which is fast assuming the characteristics of religious thought. Increasing knowledge of the causes and laws of disease, increasing recognition of the unequal health prospects of the children of the cottage and the castle, mating with class feeling, itself the offspring of envy and of a belief in the essential equality of man, have bred the great emotion not yet adequately named, which, more than anything else, helped to carry the non-German world through unbelievable sacrifice to victory. That emotion has been defined as the desire to make the world safe for democracy. This really is no definition. Perhaps we cannot define it yet, but we can see it at work as an emotion of human betterment in the great "uplift" movements, or can watch it finding expression in centres for child welfare, in schemes for housing the working classes, in the establishment of Ministries of Health, of Reconstruction and Research, in the growth of the Labour Party, in the spread of Socialism, of Syndicalism, and, incongruous though it may seem, in Bolshevism, and in the great ideal struggling to express itself

through the League of Nations. In short, new gales fill the sails, new charts are loudly demanded, and new helmsmen struggle to grasp the tillers of the ships of state.

We are at this moment in the power of a world-wide emotional storm, the full effects of which are not yet manifest. The perils of the moment enthral us. Is the armada of civilisation to be dashed to pieces on the rocks now almost beneath our bows? Are we to strike the reef and then with torn-out bottoms slide back to sink in deep water? Or, even though some ships go under, is the armada to be saved from destruction now, merely to sail to disaster on other rocks, or will it at the last come safe to port? And if the ships be lost, what of the survivors? Are they to struggle on as best they can in open boats through new dark ages and new middle ages to civilisation once more?

The issue may well be in doubt for years to come. It depends largely, though by no means exclusively, upon the medical profession. Much of the new chart that is now preparing has to do with physical health, and clearly can be accurately plotted only by men who know the achievements and limitations of medical science. Already the politician and the civil servant, alike untrammelled by medical knowledge, are becoming health experts, and are at work plotting the chart. There is great danger in this, but it is useless to cry for spilt milk. It is peculiarly useless for the medical profession to cry, for the pitcher was in their hands. If only we can round the rugged promontory of the next few years, and if the future be consciously and conscientiously prepared in the universities, in the schools, aye, and in the nurseries, and if the medical profession clearly and carefully speak the truth, so many correctly plotted points may be added to the chart of human life that the fleet of humanity will come safe to port in spite of all. We cannot hope that every point plotted will be correctly placed. We cannot hope for so much from this generation of doctors as we may rightly expect from the next, but if we could all see, as I believe many medical men in English-speaking countries do, a little further and a little more clearly than the lay world in the direction in which the emotion of human betterment is driving us, those now middle-aged might live to rejoice at the recognition of medical science as the main basis of political action, for all political action aims, nominally,

at least, to secure the health and well-being of the people. If bitter experience had not proved the contrary, it would have been pardonable to assume it unnecessary to insist that the words "medical science" mean the body of accurate knowledge concerning the effects of the material universe on human health, and not the sum of the whimsies and fashions which agitate the minds of the practitioners of medicine.

I have heard teachers in medical schools say that their whole duty to their students was to teach them to prevent disease, to treat the sick, and to understand the method of science. It may be so. I doubt it. But I am quite sure that it is the duty of the universities and colleges consciously and actively to cultivate the spirit of citizenship in the students who aspire to emerge as doctors through their portals, and if possible to make sure of that even at a risk that the technical instruction suffer. That I should hold such an opinion seems to me in my purely scientific moods almost discreditable, but the last five years have taught me many things, and the first of these is definitely to recognise how small in account and of how little power in the great movements of humanity is the scientific knowledge of to-day. I fear it may always be thus unless a sufficient number of those who have that knowledge, leaving their laboratories, come forward to bear their share of the burden of Government and to learn those lessons which responsibility for administration alone can teach, and unless a still greater number take part in those rambling discussions in press and market which in democratic countries decide policy and make legislation possible.

Perhaps I may claim some special knowledge of the results of our medical education on its civic side. Since April, 1916, I have had much to do with many doctors, and have learned that the medical profession in Great Britain, with brilliant exceptions, is in the main composed of men who are immature as citizens, and in quite a separate compartment of their being possess expert technical knowledge, too often on sale to the highest bidder. In those that have served with the Forces this strange duality is much less clear. There has been undoubted fusion, but it is still true that the medical profession, as I have seen it under the stress of war, consists in the main of men whose citizenship is as divorced from their tech-

nical knowledge as is the citizenship of the speculative builder when he jerry-builds new slums.

Frankly I was not prepared for this. Perhaps I should have been. But prepared or not, I now know that right at the very heart of citizenship, at the very centre of the greatest terrestrial interest of humanity we professors and teachers in medical schools have sinned, I hope not past forgiveness, but still a deadly sin, for we have instructed men and women to be doctors, healers of disease and interceptors of infection, and have failed to educate them to understand their duty in and to the community. As a matter of fact many a wretched medical student has had his soul, which is the organ of citizenship, killed within him by his medical training. It has never been my misfortune to meet a young freshman without a soul; in fact I have never met a young person of either sex who did not experience in some measure three spiritual emotions which for convenience may be called the manifestations of the soul. These three emotions are:

1. A desire for beauty for beauty's sake. This is the lowest of the three spiritual emotions and is often manifested by the brutes that perish.

2. A desire to benefit others, his family, his friends, his nation, humanity. In its rudimentary form this, too, may be manifested by animals low on the ladder of life. In its highest forms it is purely human.

3. A desire to know the truth. This is purely human.

If a man experience these three emotions he is alive. If they grow and flourish exceedingly he is great among men, however humble his estate or limited his opportunities. It is also to be noted, here perhaps as conveniently as elsewhere, that as the soul atrophies, its manifestations disappear in the order three, two, one, until in extreme cases nothing is left but a vestigial sense of sexual beauty which in the ascent of man surely was the rudiment of the first emotion, and still is linked with it by as strong a tie as that which binds memory to smell.

Now I am by no means sure that any education is possible, except in connection with the three emotions. Everything else that teachers can give to their pupils seems to me to be instruction. It is true that the third emotion, the thirst for truth, can appear to be satisfied by scientific instruction, but when this happens there is a

gradual atrophy of the desire for that portion of truth which lies beyond the scope of the scientific methods of investigation of to-day. Interest in ultimate truth is lost, and the victim of this disaster to a fundamental emotion becomes Prussianised. Science becomes to him SCIENCE.

It seems to be a law that once Science is SCIENCE, the emotions of human betterment and of beauty are perverted. We have seen all that in Prussianised Germany and it need not now be laboured.

The point that it is necessary to make most clear is this: In the world with which statesmanship has to deal, mass emotion is infinitely more powerful than accurate knowledge. It follows that those who would play their part in democratic states must understand the human emotions, more especially the spiritual emotions of beauty, human betterment, and truth.

The next point that must be clear is: A majority of the people have little education, perhaps because of this they have strong emotions, patriotism, love, hatred, greed, envy—the list is long—and their emotions rule the state. Because in the medical schools, we have almost entirely overlooked the study of the mass emotions, we have deprived the vast majority of our doctors of the opportunity of directing, even of understanding, the emotion currents surging round them. True, some acquire understanding later in life, but then the furnace fires of their capacity are clinkering with the years and their will to change is weakened. In the result, medical men stand largely outside the social and political movements which draw inspiration from their own science. Is it to claim too much to say that they might have been the inevitable leaders of these movements? They are not, because, with a handful of exceptions, they are quite unfitted to be. The schools have failed to equip them for life in the larger meaning of the word. With all their knowledge they are poorer than the common people.

Dans la politique il faut ne prendre rien au tragique et tout au serieux. Yet this is tragic, that the world is now moving on the greatest of its revolutions with a majority of the men who might have been its far-seeing leaders, blind and babbling of industrial unrest.

The First Act of the revolution has ended with the overthrow of the Prussianised states. The curtain is (January, 1919) rising on the Second Act. It will end with the overthrow of the Prus-

sianised individuals. How long it will last none can tell, but elemental forces are in motion and the end is sure. The Third Act must be marked by the reconstitution of society, for if that fail our civilisation dies and the attempted revolution will have ended in suicide. Failure? Success? The end is on the knees of the gods. No prophecy is possible, but this is sure: if the medical profession does not rise to the height of its opportunity, failure is, humanly speaking, certain, for the men who really know, must, if they can, guide in the realm of physical betterment not only the emotion of the masses, but the thought of the men they are throwing up to act as their leaders into the promised land, where in their vision none shall be hungry except through his own fault and none shall tyrannise over his fellows.

I notice that when one speaks of revolution, many at once picture barricades in the streets, red flags, blood, and terror. As a matter of fact most of our British revolutions have been marked by none of these things. The difficulty is that once people are convinced that the world revolution now in progress need not necessarily be bloody everywhere, they fold their hands and say, "Ah! I see you use the word revolution in a figurative sense," which is just what I do not do. Society is turning round and it can turn round and continue to exist with great profit to the majority, and without producing chaos, if all will put their hands to the wheel and keep it moving steadily in the desired direction. But if some try to push too hard and some push against the movement and some do not push at all, there may be trouble.

It would be well if all realised that the emotion of human betterment, the instigator of the world's turmoil and of the demand for change, is the child, in evolution, of mother love—the dearest instinct of the human race—and always seeks to concentrate on the future for the children's sake. It has proclaimed a holy war against the instinct of self, the fiercest instinct of the individual, and has enlisted under its banner an army of which unfortunately 90 per cent will desert to the enemy if their loyalty be tampered with by the devil of greed—will desert *en masse*, and will raise the banner of Bolshevism, and will say and honestly believe that it is the very banner under which they are now enlisted. What history will record they did depends on leadership.

In all solemnity I say, the choice before the world now is either barbarism once more after weeks, months, years, perhaps a century of struggle, or the victory of the emotion of human betterment and the reconstitution of society on a basis hard to foretell, but necessarily one on which democracy will be safe for the world. This choice was inevitable when 10,000 who were not millionaires each got one vote for every millionaire who got one, and when the universities failed to provide the right sort of leaders for the age.

I have been asked, "Why should the universities be responsible for producing the leaders?" The answer is plain and easy. Only those who have devoted themselves to the emotion of truth and in a university have learned that the limitations of science can guide those swayed by the lower emotion of human betterment, and of these only the few who are in daily contact with the poor and simple can be their leaders and can voice their needs.

There are only two bodies of university men who have this privilege—the clergy and doctors. It is one of the tragedies of our social life that the clergy, the professed upholders of the Christian ethic, have failed to provide the leaders who could have forced the world to organise itself in accordance with the commands of the emotion of human betterment—the central emotion of their religion. Is it because so many of them have been compelled to pray that all may find contentment in that state of life to which it shall please God to call them? This is just what the emotion of human betterment, as it works and transforms itself into political thought and principles, must make men regard as essentially wrong. It is clear that somewhere, somehow, the clergy have failed. There remain only the doctors, and they have failed too.

The measure of the failure of the medical profession is to be found in the revelations of the recruiting medical boards and in such documents as the Report of the Royal Commission on Housing in Scotland. If the medical profession had been using its technical knowledge in the interests of the state as a whole, it would have been insistent years ago in its demand for better houses, for better feeding, for better wages, for shorter hours of labour, not for itself, but for the toiling millions to whom it ministered. Isolated voices were heard, but the civic sense was lacking, the demand which could not have been resisted was never made. The profession had

only to organise its own knowledge and tell the truth about the condition of the lives of the workers to compel the emotion of human betterment throughout the world to force action.

I am told that the profession could not have been expected to do this, as they would not have been paid for doing it. Precisely. My whole complaint is that our universities have largely failed to educate their graduates in medicine to understand their relation to the state, and not only their graduates in medicine. The suggested excuse, if it were ever put forward as an official explanation of inaction, would be enough in itself to damn the profession. No man whose whole being is inspired by a living faith ever seeks to make great profit out of it. He is content with reasonable provision for himself and with conditions which will make health possible for his children. But surely no man seeing infants slaughtered could say, "I must be paid for giving the alarm." I know the excuses. I know how sound they are, how convincing to the individual and how bad from the point of view of the state.

In palliation of this failure it may be urged that the medical profession is predominantly male, that much of the work it has to do is not man's work, and that consequently the majority of its members can with difficulty find inspiration in their daily round. There is truth in this. A great part of ordinary general practice, the care of children, for example, though perhaps interesting in a way to men, makes a peculiar appeal to women. The instinct of motherhood teaches them to see in the child the adult that is to be. Already in the bud they understand the promise of the fruit. Unconsciously they possess that sense for the future which is the essence of the emotion of human betterment. The male instinct prompts with different whisperings, for males, in virtue of a million years of war, are fighters, and to the fighter, to-day, when he lives, and the action of to-day, are more important than the morrow, which he may never see, or than the fruits of autumn, which he may never know. And so it comes that the male is by heredity three parts equipped to fight the invading bacillus for his patient's life, while he lacks the very quality which would make him intolerant of the slow-drawn torture of overwork and bad housing displayed before his eyes. He experiences no sense of battle in dealing with these. Their results are too remote, too intangible to fire his soul. Surely

no worker by hand or brain needs to be told of the difficulty of drawing inspiration from a common task which does not chime with instinct.

Here we have touched one of the fundamental difficulties of the day, for the restless, combative instinct of the male, never more awake than now, makes it easy for the devil of greed to translate the emotion of human betterment into Bolshevism, which as a social creed is nothing but a dangerous derelict driven without chart or rudder on a voyage to nowhere. If humanity embark on that cruise, the tortured world will have no alternative but to move forward to new revolutions until either civilisation dies or the emotion of human betterment wins and somehow reforms society.

Just as in the forgotten days of the dawn man alone could never have taken the great step necessary to pass from the culture of the hunter to that of cultivator, so now the hope of safe sailing from the predatory social organization of to-day to the ordered society of our dreams depends upon the mother mind with its yearning for peace and brightness to-morrow, the children's day. It is fortunate that every man has something of his mother latent in him, and that the inspiration of leadership may still make the latent dominant, because not now, possibly never, can woman alone rule the state.

Because this is a medical occasion I have dealt almost exclusively with the responsibility of our profession for helping to guide the work of social reconstruction, but I would not be misunderstood. On no man and on no woman, proud or humble, wise or simple, does responsibility not fall. Each without regard to profession or estate has his appointed share in the common duty to secure that the charts are right, that the helmsman is skilled, and that the rudder is sound. Now, charts are as right as the wit of man can draw when they are plotted by knowledge on that durable stuff of which the instinct of the future is the warp and human sympathy the woof; and the helmsman is as skilled as the wit of man can judge when he is wise in statecraft and seeks no personal reward, but with his chart ever before him steers fearlessly, intent to assure the safety and prosperity of the realm; and the rudder is as sound as the wit of man can fashion when it is forged of the tireless will to seek justice and ensue it. Thus equipped, though the gales of emotion blow as hurricanes, shall the ship of state sail safely if God will.

ON THE TEACHING OF MEDICINE

By W. Hale-White, M.D., London

THE friend to whom these essays are affectionately addressed has taught the science and art of medicine to such large numbers of students and has always been so ardent an advocate of good teaching, for both pregraduate and postgraduate students, that it will not perhaps be inappropriate if the writer imperfectly indicates what seems to him the best manner in which to teach medicine, especially as he has for thirty-five years devoted his freshest energies to clinical teaching.

It may be said that much of what follows is in the present state of affairs impracticable, but we often do better if we fix our aim on something so high that we can hardly hope to attain it, than if we strive to reach a less lofty goal. Contemplation of the best possible conditions fires the imagination, and thus spurs us farther towards the ideal to which we never come.

In olden times, when medicine was a matter of doctrine handed down from authority, it did not much matter where it was taught, provided that learned men were gathered together, but now we know that medicine ultimately rests solely on observations of men alive and dead, and of experiments which explain and help these observations, it is clear that the teaching of it can be satisfactorily carried out only where very large numbers of men are collected. The student, from his beginning to his death, must always observe and observe for himself; books count for little in comparison with personal observation by the learner. Hence nowadays no medical school should be founded except in one of the great cities of the world, for it is impossible for the student to see too many examples of disease. If he sees great numbers of patients the outstanding features of the common diseases become fixed on his mind; he learns that no two patients, even if they have the same disease, are exactly alike, and he has an opportunity of becoming acquainted with rare diseases. Even for the beginner a large supply of patients

is necessary. Take a simple example: The teacher introduces the student to his first case of phthisis, demonstrates and explains the symptoms shown by the patient. Hardly any single case of phthisis has all even of the common symptoms, but if, during the months the student is with this particular teacher, he is shown ten or twenty other cases and his attention is directed to the differences between them, he will then have learned something really worth knowing about the symptoms, course, and treatment of phthisis.

Although medical schools should be only in very large cities, in each of them the schools should be few. Unless the population of the city is several millions, one, or at the outside, two schools is enough, for if more, the patients at each will be too few. The hospital and its attached school must in no respect be stinted in money. Nothing pays a state better than to have a high average of health among its inhabitants, and this cannot be obtained unless patients are well treated, and above all unless every facility is given for medical learning and research. To take a simple instance, what a saving it would be to the state if some means could be found of preventing measles. Sir Thomas More was hardly, in the common meaning of the word, Utopian, when he said:

"But first and chieflie of all, respect is had to the syeke, that be cured in the hospitalles. For in the circuite of the citie, a litle without the walles, they have iiii hospitalles so bigge, so wyde, so ample, and so large that they may seme iiii little townes, which were devised of that bignes partely to thintent the syeke, be they never so many in numbre, shuld not lye too thronge or strayte, and therefore uneasely, and incommodiously: and partely that they which were taken and holden with contagious diseases, suche as be wonte by infection to crepe from one to another, myght be layde apart farre from the company of the residue. These hospitalles be so wel appointed, and with al thinges necessary to health so furnished, and more over so diligent attendaunce through the continual presence of cunning phisitians is given, that though no man be sent thether against his will, yet notwithstandinge there is no sicke persone in all the citie, that had not rather lye there, then at home in his owne house."

There are two kinds of medical teaching, postgraduate and pregraduate. To be conducted efficiently they must be carried on by separate teaching and very desirably in separate institutions. Those who attend postgraduate courses require different teaching,

for they will consist of those who, already knowing some medicine, have come from foreign countries, or of those who have been in practice in their own country but wish to spend a few weeks or months in seeing how medical science has progressed since they left their medical school.

Postgraduate instruction will be considered first because it is that in which we are most deficient, indeed there is no properly co-ordinated postgraduate instruction in this country. The hospital attached to the postgraduate school must contain several hundred beds, and as part of the school there must be a hospital for infectious diseases and one for mental diseases and a lying-in charity. There must be laboratories for the professors of medicine, surgery, pathology, pharmacology, bacteriology, and clinical chemistry. There must be a hostel with a library, common room, dining hall, and sleeping accommodation for those who wish to take courses. It goes without saying that there must be all the usual adjuncts to a modern hospital, such as *x*-ray rooms, electrical department, and one for massage and remedial exercises. The whole institution should be near a public park or on the outskirts of the city so as to obtain plenty of light and air, but not so far off that the large hospital cannot be kept full.

The *professor of medicine* must be one who has shown that he can teach, conduct research, and help others to investigate for themselves. Opinions are divided as to whether he should be allowed private practice, but surely such a professor as we all desire should be so well paid that he need not do private practice. He should be a thinker who has time to think, which he will not have if he is subjected to the exhaustion of travelling, and the thousand and one worries of consulting private practice. Some say, let him do a little, but if it is understood that part of his income is derived from private practice, he cannot be blamed if he pursues it honourably and it is just the ablest professor, who would be an ornament to his medical school, who might have the largest private practice, and therefore be most likely to curtail the energies that should be devoted to his professorship. He may try honestly only to do a little private practice, but, unless he is a failure at this, it is impossible, for there will be many calls to which he will feel compelled to respond, even if at the time engaged on investigations in the

laboratory. No, the professor should be a man provided with an income which will prevent his worrying as to how to live, and which will attract a man of outstanding ability, who will be able to devote his entire energies to thinking, investigation, inspiring investigation in others, teaching, and the treatment of hospital patients under his care. Such a man should retire at sixty at the latest, as it is doubtful whether the hard work of teaching can be well done after this. The details of the teaching will depend upon the number of postgraduate students, but the professor should go round the wards and teach at the bedside several times a week, give clinical lectures, and be the head of the medical laboratory, but he will almost certainly require physicians and assistants to help him in the general wards, to take charge of out-patients, to take charge of children's diseases, skin diseases, nervous diseases, and to look after the patients in the infectious fever hospital and in the mental hospital, in connection with which there should be a separate building for early curable cases. All these assistants should teach, and ability to do this should weigh greatly in the selection of them; those who have any aptitude for investigation should be encouraged to pursue their investigations in the wards or the laboratories. All these physicians and assistants must be properly paid. It is to be hoped that some of them would be so enthusiastic in teaching and research that they would not have time for private practice, but it should be allowed, for all of them cannot become professors, and when a man's practice becomes large enough seriously to interfere with his work at the school, he must leave it to make room for someone who can give proper time. None should stay on after the age of sixty, many will go before fifty. Want of space prevents a discussion of the arrangements for surgery, midwifery, obstetrics, ophthalmology, laryngology, otology, and orthopædics, but they should be on the general lines of those indicated for medicine, and they must be first rate, since many postgraduates desire teaching in specialties; in particular it is to be hoped that there will be ample arrangements for the staff of the obstetric department to conduct labours themselves and teach thereon.

The *professor of pharmacology* must be encouraged to associate himself with the professor of medicine and other physicians who must give him the opportunity of investigating the action of drugs

on disease, and conjoint researches by the pharmacologist and the clinicians should be frequent. There should not be a professor of therapeutics. It is the duty of the professor of medicine and physicians in charge of patients to include in their teaching the details of the proper treatment. It is a frequent complaint that instruction in therapeutics is poor. This is due to two causes: Firstly, many expect too much of treatment. The wise physician knows that no treatment avails in many diseases which pursue their course to recovery or death irrespective of what we may do. If in any disease, Nature herself cures 75 per cent, any drug that is given may quite wrongly get the credit. There are those that loudly protest that this or that remedy is beneficial for a disease, although they have no knowledge of its course when left to itself. Secondly, the physician fails to indicate what therapeutic means—if any—should be used. But this is evidence that he is a bad teacher; the remedy lies in making him properly fulfil his duties to those who are learning from him. He must be familiar with and critical of all forms of treatment, and should give his hearers the results of his experience.

There is no need to go into details regarding the duties of the professors of pathology, clinical chemistry, and bacteriology. Progress in these branches is so rapid that all three professors will be fully occupied with research work, and with postgraduates who wish to learn in what way these subjects have advanced since they were students. Outside hospitals, post-mortem examinations are few, and therefore postgraduates should attend as many as possible.

The general outlines of a school for ordinary medical students will be the same as that just given for a postgraduate school, but if the preliminary subjects such as chemistry, biology, and physics are taught, there must be properly paid teachers, and there certainly must be well-paid professors of anatomy and physiology, with laboratories adequately equipped for teaching and research. When the students arrive at their clinical courses, their instruction must be derived from actual daily contact with patients; it cannot be too clinical. Let us take general medicine as an example. The following arrangements are suggested for a big school: Two hundred and twenty beds, and out-patients seen five days a week. In charge of the beds, the professor of medicine, well paid, not

allowed practice, and taking eighty beds, and two physicians allowed consulting practice, paid for their teaching, but not on the same scale as the professor, taking fifty beds each. In charge of out-patients, the professor one day a week, and four assistant physicians paid for teaching, each taking one day a week, and each with ten beds, into which they can send cases they wish to watch. The professor and the four assistant physicians will teach regularly at out-patients. Every medical student will do six months' clinical clerking in the wards, having certain beds allotted to him. For three months he will clerk to the professor, for three months to one of the other physicians; the professor will, therefore, have double the number of clerks, and should take them in two sets; visit the wards, and do thorough bedside teaching for one set on two days a week, for the other set three days a week. Each of the physicians to do bedside teachings three days a week. A medical clinical lecture to be given weekly, sometimes by the professor, sometimes by the other two physicians. These three must have been selected for their posts because they are good teachers; the professor should retire at sixty, and the two physicians at fifty, for probably by then their private practice will interfere with really first-rate teaching, and further, beginners at medicine are best taught by younger men. The professor and the physicians will give their chief attention to their own clinical clerks, but other students should be encouraged to go around with them, for the larger the audience the better the teaching. The professor must do everything he can to encourage research, and it is to be hoped that the assistant physicians in particular will pursue this. Each of them may look forward to the posts of professor, general physician, or physician in one of the special departments, which will be the same as in the postgraduate school, provided that he has proved his ability to teach or investigate. Promotion should not take place as a matter of course, indeed it might be a good thing if the assistant physicians were at first only appointed for three years.

The teaching of pathology, pharmacology, bacteriology, and clinical chemistry, and all the special departments of medicine will be much the same as in the postgraduate school.

Postgraduate students attend for a few months only, but ordinary medical students are at their school for years, and for just

those years in which they are most receptive, indeed their outlook on life then takes shape. The least important part of their education is the learning of facts. They must be taught to reason clearly, to think for themselves, to weigh evidence, to estimate properly the human side of their profession, to see the never-ceasing interest of the problems of medicine; for then their life's work, instead of being a drudgery, will be a continual pleasure. There must be organisation for outdoor games, for debating societies, where both professional and non-professional subjects are discussed. They must get to know one another and their teachers, for the friendships of life are found at this age. Every opportunity must be taken to widen their outlook, for he who practises medicine has to deal with all sorts and conditions of men. The medical school should be a corporate whole, and the student's life in it should be such that he can look back later and truly say that of his whole life, the best and happiest time was that which he spent at his medical school. There is no one who needs training for "fitness for the world" more than the medical student, who in after life will have to deal with fools, knaves, wise men, aristocrats, paupers, indeed with every kind of man and woman in their deepest sorrow and in their greatest joys, and nevertheless will have such an arduous life that he must for his own sake so train his mind that he can be happy in spite of the sorrow he will see around him.

Medical schools, both pregraduate and postgraduate, should be the fountains of advance in every branch of medicine, and should be full of workers trying to unravel medical problems. The professors should be teachers and investigators, and have the faculty for inspiring and helping research in others, and the professorships should be regarded as among the highest posts to which scientific men can attain. All the teachers should feel that they are part of an association of workers aiming to keep high the reputation of their school. Each should know the others well. In some medical schools they have kept too much apart, the clinicians in their wards, the others in their laboratories, but medical questions require many to solve them. The physician has much to learn from, say, the physiologist or chemist, who, in their turn, can learn from the physician. Team work should be fostered, and papers, each the work of several authors, should be common.

It will be said that such a scheme as is here outlined is impossible, on account of the expense, for it is essential to it, because all the professors should be so paid that men of first-rate ability will be attracted and will be freed from the worry of struggling with an insufficient income. But this is not a valid objection; money cannot possibly be better spent than in trying to promote health. Quite apart from the scientific interest of medical knowledge for its own sake, quite apart from mere humanity making it desirable to relieve the sick as much as possible, the diminution of sickness in a community increases its effectiveness, lessens the cost of looking after the sick, and can be brought about only by the provision of first-rate medical teaching and by encouraging in every way the solutions of the many unsolved medical riddles.

THE CRADLE OF THE HUNTERIAN SCHOOL

By Arthur Keith, M.D.,

Conservator of the Museum, Royal College of Surgeons, England

FOR a hundred years and more we have celebrated the anniversary of John Hunter's birthday, February 14, 1728, at the Royal College of Surgeons of England, by calling on one of the ablest surgeons of the day to deliver a Hunterian Oration. The orator is free to pick his subject from the whole realm of the History of Surgery, but such is the glamour of John Hunter's halo that from the first oration by Sir Everard Home in 1814 to the sixty-ninth, by Sir Anthony Bowlby in 1919, scarcely an orator could resist the fascination of the eighteenth century surgeon. The orators have drawn for us varied pictures of Hunter, pictures which are often splendid, comprehensive, and penetrating, but by common consent all of them pale before the vivid masterpiece limned under the northern skylight of a large dingy London studio by a young man—Thomas Henry Buckle—who knew nothing of medicine, surgery, or natural science, except what he had learned from the 10,000 volumes amongst which he lived and browsed. It was in the later fifties of the nineteenth century, when he was rapidly approaching his fortieth year,[1] that Buckle came to draft the second volume of his "History of Civilisation." It is towards the end of that volume (p. 549) that he writes as follows:

"I have now only one more name to add to this splendid catalogue of the great Scotsmen of the eighteenth century. But it is the name of a man who for comprehensive and original genius comes immediately after Adam Smith, and must be placed far above any other philosopher whom Scotland has produced. I mean, of course, John Hunter, whose only fault was, an occasional obscurity, not merely of language, but of thought."

[1] Thomas Henry Buckle (1821–1862) was born in London. His father allowed him to select his own course of education, and left him sufficient means to permit him to follow his own bent. He died of typhoid fever while travelling in Palestine at the age of forty-one.

Hunter's contemporaries placed Haller high above him, and the generation which followed regarded him as a much less significant figure in the realms of science than Cuvier; Buckle places him above those great men, and gives him a place side by side with Aristotle, Harvey, and Bichat.[2] The powerful intellect of William Lawrence gave him a place with Harvey, Sydenham, Bacon, Locke, and Newton. Benjamin Brodie said that Hunter could be most aptly compared to Newton. Still more daring is the Orator of 1851—Mr. R. A. Stafford, whose ripened judgment was that "as a man of natural genius Hunter resembled Shakespeare more than any other man"—both in the reach of his intellect and in the scope of his sympathy. My friend, Sir James Mackenzie, regards Hunter as the "Shakespeare of Medicine." If it is Shakespeare who can best lead us into the great world of human action, it is Hunter who can best guide us through Nature's limitless workshops, where the dead matter of the earth takes on the pulse of life. Nay, even in certain minor details Stafford traced points of resemblance of Hunter to Shakespeare. Both were members of a family of ten, both are said to have grown up in idleness and been addicted to loose company, and both came to commence their great careers in London—one from the banks of the Stratford Avon, the other from the farm lands of the Glasgow Clyde. Each of them became the head and front of a school born in a period when the national intellect was quickening in the sunshine of new ideals—Shakespeare in the spacious dreams of Queen Elizabeth's time—Hunter during the intellectual thirst which fell on Scotland in the earlier decades of the eighteenth century.

To mark the conditions and circumstances under which the Hunterian School was born, the school of which John Hunter became the figure-head, but of which his brother, William, his senior by ten years, was the founder, we have to spread before our eye a map of South Scotland, and trace the valley of the Clyde for a stretch of almost fifty miles—from the country town of Lanark to Greenock, with Glasgow half-way between. It was on the upland exposed country, some eight miles to the south of Glasgow, and lying fully 500 feet above the floor of the valley, that the Hunters were born and bred, but they, as we shall see, were but

[2] Hunterian Oration, 1834.

units in a wonderful band which Strathclyde gave to learning in the opening decades of the eighteenth century. Hence we have to cast our eye along the valley and note the names of the men who are to play their parts in the quiet but instructive and not uninteresting Hunterian drama. In the town of Lanark itself we shall find one of the actors, William Smellie, a reticent, studious, country practitioner, pondering, as he makes his distant country visits, the problems of childbirth. Presently we shall find him settle in London, and become a pioneer in the application of knowledge to the art of obstetrics. Fourteen miles further down the valley lies Hamilton—the ancient capital of Strathclyde—and at the time of which we write a quiet country town containing between two and three thousand inhabitants. Near by is the ducal palace of the Hamiltons; the Duke's agent, or factor, is a Mr. Cullen, but being a laird himself, he is known by his friends as "Saughs"—the name of his small estate. Saughs' son, William, has been apprenticed to a surgeon in Glasgow, and presently we shall see him established in practice in Hamilton, exchanging books and opinions with Smellie, by and by becoming the father and inspirer of the Hunterian School, and the high priest of medicine in Scotland. Long Calderwood, the home of the Hunters, lies perched on the brow of the valley, five miles to the west of Hamilton. When Cullen went visiting patients in the direction of Calderwood he had to pass through the hamlet of Blantyre, where a century later David Livingstone was destined to appear. Then eleven miles further down the valley, in Glasgow itself, there is the apothecary, John Gordon—Dr. John Gordon he is to become—senior to Smellie and much senior to Cullen, but well known to them both. It is John Gordon who sees to the affairs of the Faculty of Physicians and Surgeons of Glasgow—the corporate body which licensed and controlled the surgical apprentices and medical practitioners of Lanarkshire—for at the period with which we are dealing—the first four decades of the eighteenth century—the University of Glasgow had not yet taken medicine under its wing. It was as an apprentice to John Gordon that the "bubbly-nosed" Tobias Smollet—from Bonhill on the Dumbartonshire Leven—fourteen miles below Glasgow—cuts the first caper in his varied and vexed career. Presently too, he packs up his "spare suit of clothes, six ruffled shirts, six plain ones, two pairs of

worsted stockings and two pairs of thread dittos," and placing £10 10s. in his pocket, takes his place between the pack-saddles of the carrier's train of pack-horses and sets out for London. We hear of his examination at the Barber-Surgeons' Hall there, his hardships as a surgeon's mate with the Fleet, and presently we shall meet him again in London, the author of "Roderick Random," and a shuttle-cock in the loom of the Hunterian School. John Gordon bred literary apprentices, for Smollet was not long gone when his place was taken by John Moore—"Zeluco Moore" we may name him from his most successful novel—the father of the hero of Corunna. He, too, we shall find in London amongst the Hunterians. There, too, into this Hunterian or Glasgow cradle was drawn a boy from Kirkcaldy—from the Saxon east coast of Fife—a boy of the name of Adam Smith. William Hunter and he are to be contemporaries and share in the same influences at the Glasgow College. Here too comes the Ulster Scot, Joseph Black—to whom Cullen is to give the key which unlocks the deepest secrets of chemistry. Then further down the river where the estuary blends with the Firth, there is Greenock—a mere hamlet, but now feeling the first flow of the great tide of trade which began to break on the western coasts in the opening decades of the eighteenth century. A ship chandler there, James Watt, not only supplies the vessels which had begun to link the American colonies to the homeland, with all the outfit which ships and sailors need—but also with the instruments which navigators require. It was the desire to make such instruments that ultimately made young James Watt an instrument-maker in the College of Glasgow, and brought him in touch with Joseph Black, from whom he learned one of the great properties of steam. The man who was to transform the industries of the world was rocked in the same cradle as William Hunter, Adam Smith, and Joseph Black.

In later years we shall find John Hunter and James Watt foregathering at the meetings of the Royal Society in London. There is also another man who cuts a figure in London during the Hunterian period—James Boswell, son of the Laird of Auchinleck. He, too, as he toils after his idol, Samuel Johnson, crosses the outskirts of the Hunterian circle in London. But Auchinleck lies in Ayrshire—fully twenty miles to the south of the Hunterian

uplands. There, too, just to the south of Auchinleck there is a gardener of the name of Burns who presently is to build his small "clay biggin" near the auld brig of Doon—and give his country a singer to warm their hearts, such as they never had before or since. Lest my Glasgow friends get light-headed with the richness of this brood of men that their corner of Scotland gave birth to, soon after the eighteenth century dawned, I would remind them that the fathers of Adam Smith, James Watt, and Robert Burns were the products of my own part of Scotland—the northeast, or Aberdeenshire corner. And in case they think that Strathclyde had a monopoly of genius at the date of which we are dealing, it is well to remind them that along the northern or Scottish banks of the Tweed, David Hume, John Pringle, and John Armstrong had put in an appearance. John Pringle we shall find as President of the Royal Society in London when John Hunter was pouring out his richest tide of work; Dr. John Armstrong, poet and physician, we shall also find as an intimate friend of the Hunters, and David Hume influenced all of them, particularly Adam Smith and John Hunter. Then, lastly, in Edinburgh itself—forty-five miles to the east of Glasgow—we shall find a Sutherland Highlander—a retired army surgeon, Dr. John Monro, accompanied by his son, Alexander; Monro Primus was the man who set an example which every university in Britain had to follow sooner or later. It was the dream of the old Highlander's retired years to see medicine sheltered and fostered in the University of Edinburgh, just as he had seen it nursed and developed in the Universities of Leyden and Paris. That was the task he set his young son to accomplish in the year 1720, and he proved a fit and proper instrument for the great work, and thus, at Edinburgh, was brought into existence the first medical school in our country. We shall see that Cullen did in Glasgow what Monro had accomplished for medicine in Edinburgh, and in due course we shall find William Hunter striving in vain to work the same miracle in London. It was old Monro of Edinburgh—the far-sighted Highlander, that forged the sword that was in course of time to kill the apprenticeship system in surgery—but in the cradle period of the Hunterian School medical lore passed as best it could from master to apprentice.

We have swept an eye along the valley of the Clyde to note

the name and place of the chief actors in the drama which we are to proceed to unfold. We must now look a little more closely at the centre of our stage—Glasgow—not the modern millioned city that spreads its brimming industries along both sides of the valley, and mounts its rising banks, but the "douce toon" protrayed by Sir Walter Scott—built on the rising northern bank—a settlement of 20,000 lowland souls mixed with blood drawn from the Highland country to the north and west. That was the Glasgow which the boyhood of the Hunters knew. On a quiet Sunday morning when the wind came to Calderwood from the northwest they could hear the sound of the cathedral bell, and when the brim of the valley was reached at Dechmont Hill they could see the cathedral itself, crowning the town on the northern bank. The High Street, commencing at the cathedral, ran down towards the river, with the main buildings of the city massed on each side. On the eastern side of that steep be-gabled street is a double quadrangled mediæval block—with an extensive green behind—the "college" where the bread of learning is dealt out to the hungry youths by Latin-speaking professors. The main road from the south winds towards the city along the south bank of the river. Along this road passed trains of pack-horses until the "auld" bridge was reached by which they crossed to enter the town by the bridge on which Frank Osbaldistone foregathered with Rob Roy on a murky night. Further on, at the foot of the High Street, is the Toll-booth, to the gates of which Bailie Nicol Jarvie, guided by the lantern of his maid Mattie, made his way in the small hours of a dark Monday morning. The Bailie or Magistrate we are in search of is a colleague of the famous "wabster body"—a less exciting personage, but no less important—Bailie John Paul—who carries on the business of a maltster. We know that he is a man of substance, for he occupies the honorary post of Treasurer to the City—not that the city purse was a heavy one at that time, for only about £3000 passed through it in a year. The year in which we are to make his acquaintance, 1707, is an important one in the history of Scotland—for it was then that the Scottish Parliament went south to Westminster, and England and Scotland agreed to the common name of Great Britain. Some twenty or thirty years previously John Paul had gone into Renfrewshire for a wife and brought home a Miss Shaw, and in the

year in which England and Scotland united "for better and for worse" their daughter, Agnes, had reached the age of twenty-two—a handsome, talented lass who had acquired all the lady-like accomplishments of the time. In 1707 Miss Paul was engaged to John Hunter, "Merchant at the Kirktown of East Kilbride"—the parish in which Long Calderwood is situated. He is a late wooer, nearly forty-four years of age, double that of his bride. We do not know for certain how he met his bride. Mr. Hunter had a brother in a good way of business in Glasgow, but we suspect that the merchant at East Kilbride, as was the custom of his occupation throughout Scotland, had not only to supply his country customers with all their requirements, but also to purchase their produce. Barley was the chief produce in East Kilbride, and that was a commodity which John Paul required and which John Hunter probably supplied him with. However that may be, it is apparent that the parents of the Hunters come of provident, substantial people, well provided with worldly gear and endowments. Mr. Hunter, the "Merchant," came of a landed stock—the Hunters of Hunterstone—a family which lived for centuries in the parish of West Kilbride in Ayrshire, some thirty miles distant from East Kilbride. It is also said that his forebears owned land in East Kilbride, but neither of that nor of his descent from the Hunterstone family have I yet succeeded in finding documentary evidence.

The Kirktown of East Kilbride whence John Hunter carried his bride in 1707 is and was the centre and capital of the farming community which inhabits the upland plateau bounding the vale of the Clyde to the south of Glasgow. It was a good centre for country trade, for roadways radiate from its crowned church tower in all directions, to the northwest leading to Glasgow, 7½ miles distant, and eastward to Hamilton, snugly sheltered in the wooded valley, fully five miles away. The building in which Mr. Hunter carried on his business we do not know, but not unlikely it may have been one of the old buildings which now almost block the approach to the church gate. There at least stand the old inn and the "loupin-stane," which we may reasonably suppose Agnes Paul used when she mounted behind her husband in her younger days; even as an old lady and the mother of ten children we find William Cullen prescribing "horse-back exercise" for her.

Many of the houses along the old irregular streets are of old John Hunter's time; we estimate that it may have been then a settlement of some 1000 souls or more; perhaps there may have been 2000 in the whole parish of East Kilbride. The church, the huddled buildings round the church passage, and the churchyard, where, to the east of the church, a flat stone marks the spot where John Hunter and his spouse, Agnes Paul, lie buried, all preserve the outward appearances they presented in the year 1707, when John Hunter and Agnes Paul became man and wife.

We pass over a period of ten years—to 1717, when we find that the merchant of the Kirktown of East Kilbride has bought a small farm[3]—certainly well under 100 acres in extent—a little more than a mile from the Kirktown, on the pleasant road which winds eastwards across the uplands and sinks into the valley of the Clyde as it approaches Blantyre, whence it leads on to Hamilton. The price[4] he paid was a small one; if there was a farmhouse on the land at the time of purchase he certainly replaced it by the substantial building which now stands on the north side of the roadway, from which it is separated merely by a narrow strip of garden, and a low stone wall. The farmhouse is a substantial but plain rough-cast building facing the south; three windows let the southern sun shine into the apartments on the upper floor, two, with the front door between, serve the purposes of the lower floor. The roof is now slated, but we could guess, even had the tradition not come down to us, that it was originally thatched, for the gable ends which rise high above the level of the slates, are cut by steps—"corbie" steps—leading up to the bare squat stone chimneys which finish the gabled ends of the house. On entering at the front door, a passage leads right and left—on the left to the kitchen—an apartment of some 14 feet by 14—with traces of a great open fireplace designed for the time when peat and wood were the staple fuel of

[3] Miss Helen Hunter Baillie, the living representative of the Hunter family, with great liberality, placed at my disposal the various title-deeds relating to the estate of Long Calderwood—which with certain additions made by William Hunter has descended to her from John Hunter, Senior. The present estate comprises 177 acres and is made up of four parcels of land—the two chief being Over Calderwood, the original purchase of John Hunter, Senior, and Calderwood Logan, which William Hunter bought and added to the original estate in 1758. In the original deed of purchase John Hunter is described as "Merchant, Kirktown, East Kilbride." In my account I have proceeded on the supposition—which I think reasonable—that his designation was the same at the time of his marriage.

[4] 2677 merkes, 5 shillings, 24 pennies, which in sterling represents a sum of £147. The wage of a Scottish farm labourer at this time was about £5 per annum.

Scotland. On the right we pass into a long narrow room—panelled on the side opposite the window. The panels, however, will swing open and reveal two built-in or "box" beds. Between this bedroom-parlour, which measures about 18 feet by 14, and the kitchen, is an intermediate small room or closet. The stone stairs, which face us as we enter at the front door, lead us up to corresponding apartments—the small bedroom over the kitchen being the apartment occupied by Mr. and Mrs. Hunter—the room in which William and John Hunter were born.

I have been somewhat minute regarding the house at Long Calderwood, because it tells us a great deal. Clearly it was altogether out of proportion to the size of farm on which it was built. The long low stone building which abuts on the western gable of the house provides a scullery, a "bothy" and stabling for five horses, is clearly of later date; so is the small coach-house and great cow-byre behind the dwelling-house. But the barn, with its loop-holed and slotted end towards the road, its doorways on opposite walls, between which the corn was threshed by flail and winnowed by hand—is certainly part of the farm-steading which John Hunter's father built.

We infer, therefore, that John Hunter, Senior, in the year 1717, when he was fifty-four years of age and the father of six children, made up his mind to withdraw from business, and as is customary with men who have been successful in the country towns of Scotland, became a leisured farmer. It is also certain that without private means the farm could not carry the establishment thus placed upon it. The year following the arrival in their new home—on May 23, 1718—a seventh child was born—William. Then followed Dorothea—destined to far outlive all the other members of the family, and become the mother of Matthew and Johanna Baillie. Then Isabella ("Tibbie"), whose death we shall have to chronicle presently, and then on the night of February 13, 1728, John Hunter, the tenth and last, commenced a lease of life which was to terminate sixty-five years later in that stormy scene within the Board Room of St. George's Hospital.

John's arrival marks a definite point in the Long Calderwood household. Its head was now sixty-five years of age, a clean-shaven man, with sharp, clear-cut features which William inherited, and a

peculiar eye with a curious piercing gleam in it, but careworn withal and feeling the weight of a growing family. The year before John's birth we find him straightening the marches of his little farm and fencing the fields—so that a herd boy became less necessary. The year after John's birth is marked by a significant transaction—fifteen acres of the farm are sold to Neill Campbell, Principal of the University of Glasgow (he was principal from 1728 to 1861, and at his death William Hunter bought back the fifteen acres). The reason of the sale we can guess, even if we did not have it as a direct statement. The family at Long Calderwood was growing up. The first-born—who also was named John—died when fourteen; the second and third died in infancy. The fourth child—Janet—was now a handsome girl of fifteen, and we may be sure Mrs. Hunter demanded for her the education and advantages which she herself had enjoyed. Janet, we are to find, is to make an unfortunate match with the genial, engaging, but unstable Mr. Buchanan, timber merchant in Glasgow. The next and fifth was James Hunter, the cleverest of the family in William's opinion. He was three years William's senior, and that is a circumstance which influences a younger brother's opinion. At the time of the sale of land, James was fourteen years of age; he was a witness to the transfer; he was already, or about to be, indentured to a writer to the Signet in Edinburgh, and the sale of land may be connected with the money needed for his settlement. We shall see that so far as his welfare was concerned, the money was spent in vain. Then, sandwiched in between James and William is the favourite sister of all, Agnes ("Nannie"), whose sudden and tragic end lies only a few years ahead. Then came William, trudging daily to the school at East Kilbride, and we have no doubt at all a diligent, clever, and favourite pupil of his master. That reputation he is to maintain in every phase of his successful career. Then came the two young girls, Dolly and Tibbie, and lastly John, puking and puling on his mother's lap, a woman of forty-three.

Having thus seen the Hunter family established at Long Calderwood, and one boy launched on a career, it is now time to take up and follow the fortunes of the founder of the Hunterian School. At the beginning of October, 1731, when he was in his fourteenth year, and holder of a bursary worth £10 per annum, for a space

of four years, although the curriculum ran to five, and with the pulpit of a Scotch Kirk in the background as his ultimate goal—William set out for the University of Glasgow—the "College." The bell rang at seven o'clock in the morning for lectures, and the gate was closed ten minutes after the bell ceased. Clearly this finely made but small slip of a boy could not trudge the seven long miles morning and evening between the College and his home; like other students he must go into lodgings, or seek shelter in the house of his uncle in Glasgow. At week-ends, when he goes home, his mother will see to it that he has a supply of farm produce to take back with him, and so he passes through the five years—from his fourteenth to his nineteenth, Latin being the chief subject of his first year, Greek of his second, Logic of his third, Moral Philosophy of his fourth, and Natural Philosophy of his last and fifth. All the professors lectured in the Latin tongue except the Professor of Moral Philosophy—Francis Hutcheson, an Ulster Scot, who had flung the languages and conventions of the ancient world behind him, and had set out to initiate the budding youth of Glasgow into the capabilities of the English tongue, and the urgent social problems of the modern world. The aim of his philosophy, he said, was to give the greatest happiness to the greatest number. He was a precursor of David Hume; he set Adam Smith, William Hunter's junior contemporary in the University, on his road to the "Wealth of Nations," and sent William Hunter home to Long Calderwood, when his fifth session closed in March, 1736, with his articles of faith sadly shattered. There was talk then of his becoming a schoolmaster at East Kilbride.

William now took the most important step of his life—or more likely William Cullen, the family physician in Hamilton, took it for him. At any rate in the autumn of 1736 he joined Cullen as a pupil—or apprentice. So far as we know there was no indenture, agreement, or fee; two kindred souls had come together. William Cullen was then in his twenty-seventh year, William Hunter in his nineteenth. Each of these men, we shall see, had an unerring instinct for the recognition of ability—but in the present partnership Cullen's is the master-mind. If ever there was a case of Jonathan and David in the medical world it was in the wooded valley of the

Clyde between the country surgeon of Hamilton and William Hunter from the neighbouring farm of Long Calderwood. Cullen was a man built on big lines, in body as well as in mind; easy-going, judicious, beginning many things and finishing a few of them. William Hunter was small in body, with an alert mind which cloaked a certain degree of nervous self-consciousness with an exceedingly pleasing address and lively conversation. But where did Cullen get his greed for knowledge? For we find him gathering the latest publications on medicine from home and abroad, noting the latest advances in chemical discovery, applying himself to experiment, keeping accurate record of every case within his practice—just as did his senior neighbour, William Smellie, in the town of Lanark, fourteen miles further up the valley of the Clyde. The truth is that in Cullen we have one of the rarest species of the man of science—a masterless master. It is true that at the age of seventeen—that was in 1727—he went to Glasgow and was apprenticed to a surgeon-apothecary there for two years; then he disappeared in the south—three years in London—on a voyage as a ship-surgeon, then in an apothecaries' shop, returning to carry on an irregular practice in Hamilton or its vicinity for a year or two more. Then, in October, 1734, when in his twenty-fourth year, he went to Edinburgh University and took the full medical course given by Alexander Monro and his colleagues—a complete course extending from October to May, in which Monro treated of the anatomy of man and beast, of physiology, surgery, and bandaging. The Edinburgh Infirmary had just been built, and for the first time in that city students could follow physicians and surgeons round public wards and watch methods of treatment. In the spring of 1736, after spending two winters in Edinburgh, Cullen returned to Hamilton to settle definitely to practice there, but even then with the resolution that some day he would effect in Glasgow University the medical revolution which Monro had wrought in Edinburgh some fifteen years before. Thus, when Hunter came to live and work with Cullen in the autumn of 1736, he found Cullen full of the spirit that was awakened in Edinburgh by Monro.

Cullen was already grappling with the system of medicine which the great Boerhaave of Leyden had imposed on the medical practitioners of Europe, examining it, taking it to pieces, studying the

teaching and practice of other leaders in medicine, and building up, by his own thinking and observation, another system more in keeping with the results of his experience. He had come to the conclusion that if the secrets of disease and cure could be unveiled, there was only one kind of knowledge could do it—a knowledge of chemistry—a knowledge of the elements out of which the living body was built up. He was under the patronage of the Duke of Hamilton, who provided this country practitioner with a chemical laboratory. He had his experimental garden for medicinal plants. He had a practical knowledge of agriculture and applied his knowledge of chemistry for the improvement of husbandry. It was when William Hunter was with him that he sat on the bench as "Bailie" Cullen, and showed his sound judgment by refusing to shoot down the hungry mob which scoured the neighbouring farms for the grain which farmers were hoarding for a rise in prices. He made the rioters pay a fair price and then handed it to the angry hoarders. He was a fine, great-hearted man who imbued William Hunter with the learning of liberal medicine.

Thus from October, 1736, to October, 1738, William Hunter lived in Cullen's house, and was taught the rudiments of the art of healing by the fittest medical brain in all Scotland, and was fired, too, by the ideals and aspirations of a great mentor. What was done in Leyden and Edinburgh could be done in Hamilton and Glasgow. Cullen knew the merits of actual experiment, but his hands were clumsy and his natural inclination was to observe, think, and explain. William Hunter, on the other hand, had neat, workmanlike hands, fit for all kinds of manipulation. Hence grew up between them the idea of a partnership, Cullen as physician, William Hunter as surgeon. To carry out the scheme William spent the winter 1739–40 at the University of Edinburgh, attending Monro's lectures and learning from him not only the anatomy of the human body, the operations of surgery, the application of bandages, but an art in which he was to become a master—an art then taught openly, but now almost forgotten—the art of injections and of making anatomical preparations for lecture purposes. Monro had learned the craft from Cheselden in London—but above all at Leyden—where Ruysch had brought it to its highest point of perfection. Thus it came about, when William returned to Hamil-

ton in the early summer of 1740 he brought back not only a knowledge of medicine and surgery, but a practical knowledge of anatomy —not of dissections, for at that time preparations had to serve the lecturer's turn—and of the outfit which is needed by a teacher of anatomy. He owed much to Monro primus, a debt he reluctantly acknowledged in after years. On his return he found his old neighbour at Lanark, Dr. Smellie, had departed, and news had come that after a period of studying the obstetrical practice of Paris, he had settled in London to teach the science of midwifery in a way that it never had been taught before. Then, when the harvest of 1740 was garnered in the valley of the Clyde, Cullen agreed that William should spend the winter in London, following the medical practice of the metropolis, and in the spring of 1741 return to take his place as surgeon in the partnership. In the month of October, William set out, then in his twenty-third year. A letter which came from London a month later—for it took then fourteen to eighteen days for letters to come from London to Hamilton—tells us of his journey southwards. He saw grain rotting at the Pier of Leith, as he went on board the London-bound schooner on a Sunday night—October 25, 1740. On the following Friday, when his ship, with many others riding at anchor, were waiting a fair wind to take them up the Thames to London, a sudden and terrible storm swept across the ships and played havoc with many of them—but on the following Tuesday, after a voyage of ten days, all told, William reached London. He found a miscellaneous assortment among his fellow-passengers. "I had the good fortune," he wrote—apparently to Cullen, but the address is missing from the letter—"to become a kind of favourite with the first set . . . notwithstanding some crosses of Providence I lay under . . . there was a number of the second rank in the cabin." What the nature of the crosses were we do not know, but we shall find that William has always an eye on the "first rank." We find that he lodges at "Mrs. Gray's over against the King's Arms Tavern in the Strand, near Charing Cross," that he has just come "from Mr. Smellie, who seems very kind," and that to-morrow he is to call on Mr. Pringle.[5] Later news came that he had the good fortune to become an inmate of the family

[5] Dr. James Pringle, afterwards Sir James Pringle, President of the Royal Society from 1772-1777.

of the most distinguished anatomist in London, Dr. James Douglas, a Scotsman who had been settled there for forty years, and was now a man of sixty-five labouring to finish a great atlas on osteography.

In the spring of 1741, when William Hunter ought to be retracing his steps to Hamilton, we return to Long Calderwood to note certain events which are occurring there. The farmer is now an old bent man of seventy-eight, his wife, twenty-two years his junior, is fifty-six; six of their children are at home—for we find the eldest son, James, there, now a man of twenty-six, talking of entering the Army, his legal training having apparently failed to gain a livelihood for him. The eldest daughter, Janet, the future Mrs. Buchanan, is also there—a handsome woman of twenty-eight; Agnes, just younger than James, and the "flower" of the family, is ailing. The two girls "Dolly" and "Tibbie" are reaching womanhood, while the auburn-haired young "Johnnie," aged thirteen, is proving anything but a lad of promise. As a pupil under the master at East Kilbride he has proved an altogether unpromising scholar: his niece, Johanna Baillie, earned in later years the same sort of reputation—stupid at books, but uncommonly quick in observing what was happening in the world round them. He had abandoned school, this boy of thirteen, and had apparently become his own master in the farm-house at Long Calderwood. Nor was he a favourite at home, except with his doting mother, who saw excellencies in him which no other member of the household could see. He was plainly being pampered and spoiled, and met reproof and restriction with bouts of sulking and weeping. Tears were always near the surface in John Hunter's emotional moods. In the meantime letters are coming from William painting his prospects in the Douglas household and in his "darling London" in the rosiest of hues. He clearly wishes Cullen to give him his liberty, and Cullen is not the man to stand in the way of a young man with an ambition.

Meantime the Long Calderwood household is rent by a tragedy. On a day of March, 1741, James Hunter mounted his father's nag "Budy" and taking his sister Agnes up behind him, set out to the Crocketstone in the Barony of Hamilton, to exchange "Budy" for "John Hamilton's mare—of which we were to have the loan in our journey to Newcastle," the "Sabbath following" being the

day on which they were to set out. When they alighted at James Hamilton's, Agnes felt faint—so faint that she had to be carried in and put to bed in the farmhouse. She grew worse, and James rode for the family friend and physician, Cullen. Agnes pleaded so much to be taken back to Long Calderwood that a cart was obtained—a bed was placed in it, but Cullen had scarcely lifted Agnes in his arms to place her in the cart when she expired. It was a merry couple that set out on horseback for the Crocketstone on Friday morning; it was a heart-broken brother who followed the cart which bore the body of the beloved sister back to Long Calderwood on the Saturday night. "Let your grief have free rein," said Cullen to James, who sought to stifle his tears. His first duty is to let his younger brother in London know what has happened, and when he sits down in Cullen's house—where he had apparently taken up his abode—to write the letter, he advises William to let his tears flow, "for sorrow, chastened, turns sullen, sinks down on the heart, and preys on it." He closes his admonition thus: "Take care of your health, my dear Willie, forget not to pray to Nannie; imagine you have a sister in Heaven." Heaven is a word often on the lips and in the minds of the two elder brothers, but you will search young Jockie's mature writings without finding it mentioned once.

The year 1741 was destined to lay a heavy hand on the household at Long Calderwood. The tragedy just touched on happened in the spring of the year, and later in the autumn—on the last day of October—the head of the household stoically resigned the burden of life which he had borne for seventy-eight years. Through the summer he had expected William's return; he longed once again to see him, and to know that he had returned to Hamilton to carry out his promise to Cullen. Three months before his death he sat down in the home at Long Calderwood and wrote a letter to his son in London, and as we look over the old man's shoulder and watch him indite this missive, it is difficult to keep the eyes dry. He is under no delusion as to the frailty of his tenure of life: "I surely must soon expect to be beyond this side of time," he writes: his weakness and his dire sufferings from "severe fits of the gravel" tell him that the end of his lease is at hand; he would like to see his son, but did not wish to stand in the way of his advancement.

Further financial help was impossible; for he had already given more freely than his resources and responsibilities to the rest of the family justified. He counsels William to think well as to the future: with Dr. Cullen, a sure livelihood and honourable future awaited him. With Dr. Douglas in London his future was uncertain enough. But when death came, William was still in London; domestic ties and social duties, we shall find, have to be sacrificed in William's life, to the calls of professional success. Dr. Cullen had to look for another surgical partner, and found one in Thomas Hamilton, the younger brother of Robert Hamilton, then filling a nominal Chair of Anatomy in the University of Glasgow. Three years later, in 1744, Cullen moved from Hamilton to Glasgow to lay the real foundation of a medical school which was destined to make a deep impression on medical history, and to make of Joseph Black the greatest chemist that Scotland has ever produced.

Having thus seen William Hunter settled in London, and already planning the foundation of a medical school—the first which London ever had—we now turn to watch the progress of "Johnnie" or "Jockie" at Long Calderwood through those critical years which lie between the fourteenth and twenty-first of a young man's life—from October, 1741, to October, 1748. Soon after the death of Mr. Hunter, James, who had become the head of the household, joined William in London to devote himself to medicine, but at the end of the winter 1742–43 had to return to Long Calderwood, suffering from phthisis, from which he died in 1745. In the meantime other changes were affecting the household. The youngest sister, Isabella ("Tibbie"), three years older than Johnnie, died in July, 1742. The letter, which William sent home a month before her death, tells us something of the life at Long Calderwood. We find William interested in the fact that the farm mare has a foal at foot, and he hopes that "the mare's milk and the foal together will surely recover her, for you know she likes foals and calves." The love of animals was deep in the hearts of the Hunter boys and girls. "Tell her," William continues, "she must write to me about the white Hamilton 'stirk' (an ox of the famous primitive breed protected by the Duke of Hamilton), and that James and I will pay her a visit as soon as we have got our pockets full of gold to buy her a country seat and give her white horses or other things she

wants." Very soon after that letter reached Long Calderwood poor "Tibbie" was laid to rest in the churchyard at East Kilbride. Then came Janet's ill-fated marriage and her settlement in Glasgow as the wife of the timber merchant, Buchanan. Thus by the end of 1745 the farm household has been reduced to three—Mrs. Hunter, a woman of sixty, her daughter "Dolly," aged twenty-four, and "Johnnie," now in his eighteenth year. On the farm itself there will be a horseman to drive the pair of horses, a labourer to look after the few head of "black cattle," the breed which the Hunter brothers are ever referring to, and perhaps a small flock of sheep; a maid will suffice to attend the house and milk the few cows kept on the place.

It is most unlikely that John Hunter's youth differed from that which was usual then, and still is, on a Scottish farm, particularly a small one. In spring he will have to lend a hand in the sowing and in the autumn will have to join the reapers as they set out sickle in hand. He will have to do the hundred and one little daily duties which a farm life demands. At that occupation an intimate knowledge of living things sinks deep into the observant mind; youth drinks in, from life on a farm, an education which no other condition in early years can give. In later years, when at the height of his fame, Hunter noted down his recollections of these youthful days:

"When I was a boy [he said], it was a little reading and writing, a great deal of spelling and figures; geography which never got beyond the dullest statistics, and a little philosophy and chemistry as dry as sawdust, and as valuable for deadening purposes. I wanted to know about the clouds and the grasses, why the leaves changed colour in the autumn. I watched the ants, bees, birds, tadpoles, and caddis worms. I pestered people with questions about what nobody knew or cared anything about. They wanted to make an old woman of me, or that I should stuff Latin and Greek at the University (James and William would certainly press those studies on him), but these schemes I cracked like so many vermin (lice) as they came before me."

A wilful young farm boy, this John Hunter, who is determined above all things to pick his own course in life. And yet we suspect that this boyish recollection of clouds, grasses, bees, birds, and caddis worms is tinged somewhat by an ethereal reflection scarcely native

to Hunter's mind. When we turn to his works we find much more homely and concrete instances of his youthful observation. He has noted minutely the manner in which horses rise, forelegs out first, and then the sudden effort which allows them to plant their hind legs squarely underneath the body to reach the standing posture. The cow, he observes, has a different and more leisurely mode of rising—hind limbs first, fore limbs afterwards. He has noted all the differences between the stallion's head and eyes and the same parts in the work-horse. He has analysed the points which differentiate the ox from the bull—a miracle wrought by castration. He knows about the cow which holds up her milk when her calf is taken away, the variations in the quality of the milk as the udder empties, the remarkable character of the milk which follows calving—all of them puzzles which are to receive an explanation in later years. His observation and experience are to lead him on to the discovery of the sphincter muscles which guard the ducts in the teats, and the reflexes which regulate the action of the milk sphincters. He noted, too, how strange oxen just added to the herd in the field are treated at first as outcasts, but if the stranger and herd are driven to a fresh and unfamiliar pasture, then all enmity ceases. He guessed there was something in common between the casting of hairs and shedding of leaves, for he was familiar with both. He had noted the curious action with which rabbits use their hind limbs and the close manner in which they could eat the grass on the bents round Long Calderwood. Horses with cutting teeth above and below could not crop the grass so close to the roots as the ox, with its toothless premaxillary gum. He had studied the economy of the bumble bee and the habits of the house-martins which built their nests in the window corners of his home; in the "craw woodie" near by he saw, in the behaviour of the breeding rooks, points of resemblance to the habits of human society. The fowls in the farmyard gave him constant food for mind as well as body—the note of outspoken satisfaction—of pleasure—with which the laying hen announced the safe delivery of her egg, the behaviour of the cock, the miracle of the newly hatched chickens, their manner of feeding. He must have been familiar with cock-fighting and dog-fighting, but he speaks of such sports as if they were matters with which he was not in sympathy. Horses, dogs, and cats were his daily companions.

He noted the manner in which the various animals suck or lap water, the short-lipped lapping and the long-lipped sucking. The goat, he noted, sometimes sucked, sometimes lapped. He knew how cattle, gorging themselves on luscious pasture, wet with dew, became so distended, so "hoven" with wind, that a knife had to be driven into their stomachs to give relief. The white Hamilton cattle or "stirks" with their black muzzles and spectacled eyes spring to his memory when speculating on the meaning of pigmentation; he noted that all foals have the same colour of iris. In the winter, when snow lay deep and long round the homestead, flocks of birds sought shelter and food in the scanty corn-yard of upland Calderwood, and often they would fall down stiff, dazed and numb from cold and exposure. His experience in treating such patients by the kitchen fireside, seeking to restore them to life again, taught him a lesson which had a deep bearing on his life's practice as a surgeon. From that experience he drew the inference that in cases of exposure the flicker of life may be blown out by vigorous treatment and can be again fanned into flame only by using the gentlest and most gradual methods of recovery. He noted, too, how the droppings of the farm animals changed in consistency and colour with the nature of their food. We find him, when in practice in London, cross-examining a farmer in a manner which shows a close intimacy in all the practical details of farm management. "He was not destitute of warm affection," said his sister, Dorothea, who had the best of opportunities to note the habits of his boyhood. "He had great neatness of hand and a quickness of perception in anything regarding machinery." The little farm at Long Calderwood is John Hunter's University: there, with his eyes and ears as his professors, he learned the principles of Animal Economy.

During these years news was coming from William in London of the death of his patron, Dr. James Douglas, of a winter spent in Paris with the young profligate, James Douglas, Junior, of the opening of a medical class—the successful establishment of an anatomical school, of William's rapid rise to place and fame in the great metropolis. It is said, and very likely it is true, that for a year or more John went to live in Glasgow with his unhappy eldest sister, Mrs. Buchanan, and worked as a cabinet-maker in his brother-in-law's yard. No doubt he would have been an excellent

cabinet-maker, but decidedly not an enthusiastic one. He certainly had not been out of his brother William's memory, for in the early years in London William prays that success may reward his efforts in order that he may lend assistance to the folk at Long Calderwood—particularly to his brother "Jockie." And now the time has come when such help is needed. When the harvest of 1748 was ripening, and a peace had fallen on the country after the long wars of the Austrian Succession, a move was made—by whom we are not certain. John was well into his twenty-first year, a shortish man—5 ft. 2 in. in height, with broad shoulders, full, deep chest, and short neck, strong and active, but with no settled future. It is said he was proposing to enlist if an application he had made to his brother William was unsuccessful. It is not unlikely that Cullen played the good Samaritan now as on many another occasion. Before William set out for a flying visit to Leyden and Paris in August, 1748, he sent his brother an invitation to come, and no doubt an enclosure or draft on some merchant in Glasgow to provide the necessary means.

So it came about on a morning early in September, 1748, when harvest was in full swing in Scotland, we find John, booted and spurred, mount his nag, and turning its head along the road to Blantyre and Hamilton, wave his hand to the two lonely women standing by the doorway of the farmhouse—his mother, now carrying the weight of sixty-three years, and his sister Dorothea, a woman of twenty-seven. He is soon out of sight as the road bends into the valley where he is to be joined by a Mr. Hamilton—Stephen Paget says a Mr. Francis Hamilton. I have more than a suspicion it was Mr. Thomas Hamilton—Dr. Cullen's partner—the younger brother of Dr. Robert Hamilton, professor of anatomy in the University of Glasgow. We know, at least, that Thomas Hamilton went to London then and studied and dissected with William Hunter during the winter of 1748–49, and afterwards succeeded his brother in the Glasgow Chair. Whichever Mr. Hamilton it may have been, our two young friends "haud sooth." We do not know the route they followed, but there was really only one—the route which Tobias Smollett took in 1739, and the one which James Watt took in 1754—the road which led the travellers across the valley of the Tweed at Coldstream and thence on to Newcastle. Then the great North Road through York and on to London. Whether they rode the same

horses all the way and sold them at the close of the journey, or whether they posted we do not know, or care. The journey would last at least twelve days—including a couple of days to rest, and would cost the Dick Whittington of surgery some £10 in hard cash.

Having thus seen both brothers launched in the uncertain sea of London life, we again return to watch events at Long Calderwood. The two women at the lonely upland farm are hungry for news of the outside world, particularly from the two boys in London. In the summer of 1750 their loneliness was broken by the arrival of William from London, on a brief visit—the first he had made since he went on board the schooner at the pier of Leith in 1740—the last he was ever to make to Scotland. He renewed his acquaintanceship with Long Calderwood, Glasgow, and Dr. Cullen—pleased to find that the reputation he had earned in London had reached the land of his nativity. Glasgow University made him a Doctor of Medicine, and the Faculty of Physicians and Surgeons an Honorary Member.

When William's brief visit was over, the kind-hearted Dr. Cullen, now Professor of Chemistry as well as physician in Glasgow, takes the opportunity of visiting Calderwood whenever a case brings him along the seven-mile road that leads upwards to East Kilbride—particularly when he has had a letter from "dear Willie" —sometimes with a little gift enclosed for Mrs. Hunter at Long Calderwood. Mrs. Buchanan's death in 1749 narrowed the family still more, and in 1751 Dr. Cullen finds his visits to Long Calderwood really necessary. Mrs. Hunter is suffering from some abdominal complaint. It proves to be cancer of the stomach. Before the diagnosis is fully made Cullen seeks "to engage her in exercise." She tried horseback exercise, then riding in a car, lastly the more gentle going of a cart—but all is in vain—every form of exercise pains her. "She says nothing about Johnnie coming down, but I know," writes Cullen to William, "that in her present condition it would have pleased her much if he had." John is his mother's darling—not the elder and flourishing brother, William. William acknowledges this letter from Cullen with all the respect of a junior to a senior. "Dear Sir," William writes, "I cannot consent to her request this season (it was the month of August with the busy winter session coming on in London) for my brother's sake, for

my own sake and even for my mother's sake. It would be in every way a bad scheme. It is a whim begot of weakness and low spirits. Pray take an airing now and again on the Kilbride Hills." We see that family duties have to give way to the calls of business in the programme William has marked out for himself and for his brother. In October Cullen again writes to "My dear Willie," telling him that his mother complains of his forgetfulness in not writing to her and that her condition is much worse. Further, that if death should occur he would see that the last respects were paid to Mrs. Hunter and that Mrs. Cullen would shelter Dorothea until he knew William's intentions as regards his sister. Mrs. Hunter died on November 3, 1751, and Dr. Cullen was as good as his word. At every turn he shows a noble and unselfish heart. On receiving the news of his mother's death, William tells Cullen that he is "very unhappy about neither he nor John being able to be present at their mother's death, but it was impossible." The "only comfort I can procure myself on such a melancholy occasion was recommending her to my friends, and particularly to you." Rather a Pecksniffian phrase—but as I said before when domestic and public business clashed, it was William's domestic affairs which had to give way. In the spring of 1752 John Hunter revisited Scotland and Long Calderwood for the first and last time. He carried his sister Dorothea back to London and never again set foot in Scotland, not for want of will—but for want of leisure.

THE OSLER LIBRARY

By J. Y. W. Macalister, M.D.,
Secretary and Editor Royal Society of Medicine

THE other day I was "assisting" at the unveiling of a fine cast of the famous "Hope Asklepios," which now provides a noble decoration for the principal reading room in the library of the Royal Society of Medicine. Making the necessary arrangements and the time occupied by the ceremony made such a hole in official hours that I had to take home with me a larger batch of proof than usual, and, as frequently happens, the interest of the work made me forget time and space, and it was only in rising to rekindle a cold pipe that I discovered it was nearly 2 A.M., so I put aside my proofs, relit my pipe, and sat down for a little quiet thinking before going to bed.

A sudden ring of the telephone brought back memories of raids and night calls, but on going to the instrument I heard a voice that I thought familiar but could not identify. "You are wanted at once at the Osler Library. The committee has adjourned until you can come, and we are sending up one of the staff cars for you." I murmured something about the lateness of the hour, and said I should be ready. In a few minutes a haughty-looking chauffeur drove up, helped me in, put a magnificent fur rug over my knees, for the night was cold, and drove off in the direction of the Regent's Park. He stopped at a lodge gate which gave entrance to a large enclosure, and pulled up at the portico of a magnificent building which seemed strangely familiar, and yet I could not recall where or when I had seen it.

It was built in the form of a quadrangle, with a great open courtyard in the centre, in which was a noble marble statue. At first I thought I recognised it as the "Hope Asklepios," but going closer I was startled to observe that while in every other respect apparently a copy of the Asklepios, the face was that of our revered friend and teacher William Osler. Everything was so strange that

I did not at the time even think it odd that on gazing at his face, his characteristic smile, which we all love, was a *living* smile, and I could have sworn that one of those wonderful eyes solemnly winked at me.

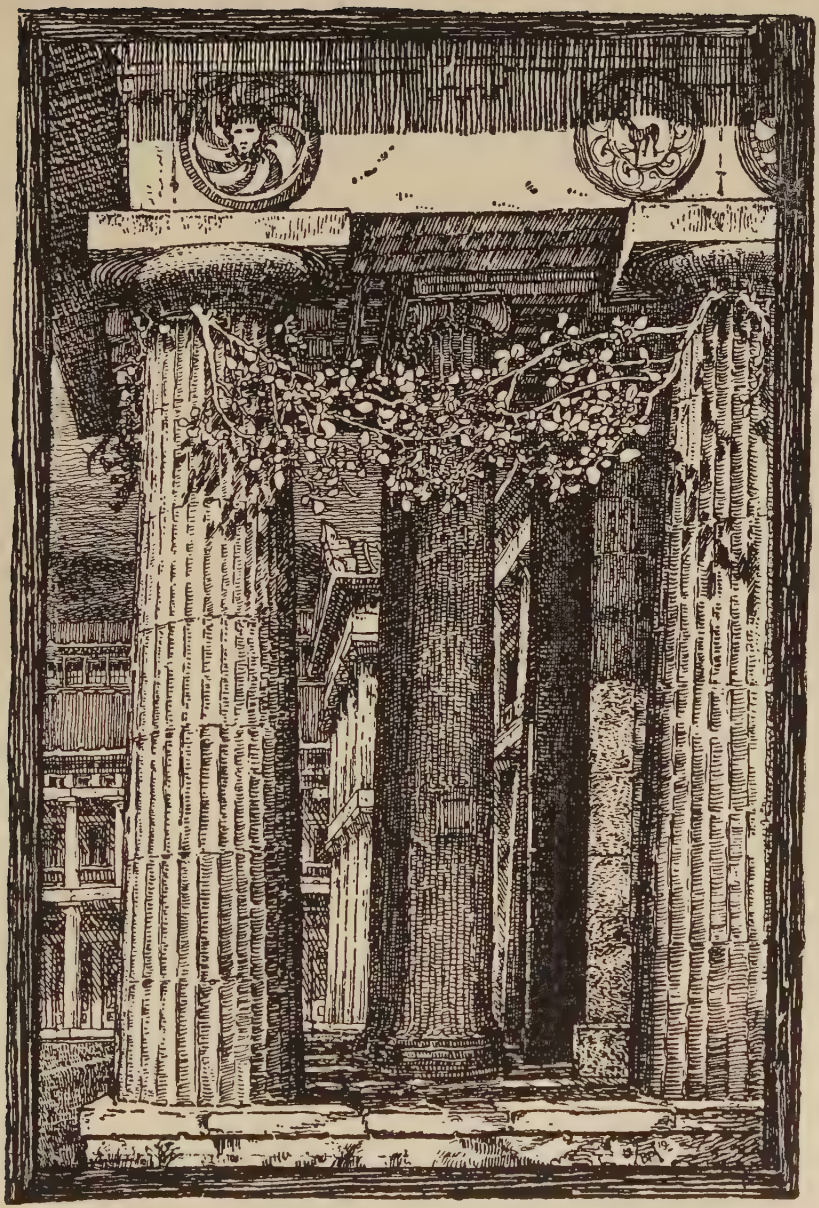
I suddenly found by my side an elderly gentleman who introduced himself as the Bibliothecarius-in-chief, and with grave dignity welcomed me on my first visit to the great institution of which he was proud to be the head, and proudest of all because it realised the ideals of that great benefactor Osler.

"And yet," he added, "the realisation of the scheme is in some respects entirely due to yourself, and I have been deputed by the committee to take you over the entire building and invite any criticisms you may have to make before the ceremonial opening."

It all seemed curiously puzzling, and yet somehow "all right," and I told him how delighted I was, but that if Osler were pleased, it was not likely I would be able to suggest any improvements.

He began by asking me to observe the stately Greek architecture, cleverly adapted in the matter of windows, lighting, and ventilation to meet modern demands. He then led the way inside to a great circular entrance hall, lighted from the top of a lofty dome which reminded me of the Pantheon at Rome. There was only one light, at the top, which at first seemed too small for such a vast hall, and yet illuminated the whole space perfectly. I guessed the opening was covered in by glass as a concession to English weather, but it was so cleverly done that it seemed to be open, and my guide explained to me that at night the light was equally good, provided from outside by a powerful searchlight.

In the spaces between the corridors opening out of the central hall there were numerous marble statues, which my guide informed me had been provided by the greatest artists of all the civilised nations that had contributed in any way to the advancement of Medicine, and pointed out with particular pride the latest gift, which had been received from the King of the Hedjaz, a noble image of Avicenna, the work of a young Arab sculptor, who, he assured me, would very soon be recognised as one of the greatest artists the world had ever known. To my surprise and delight I recognised effigies not only of the past, but of some of the present masters of Medicine. Of course Æsculapius, Hippocrates, Galen,



"The Portico of a Magnificent Building which Seemed Strangely Familiar."

and Celsus were there; down the ages with Harvey and the Hunters to Lister, Pasteur, and, as my guide explained, by the special request of Osler, living men who had done most for the history of Medicine, such as Norman Moore, who was figured as presenting his monumental "History of St. Bartholomew's," D'Arcy Power, Raymond Crawfurd, Cumston, and the indefatigable Singer.

My guide, taking out his watch, remarked that we should just be in time for breakfast with the staff, and led the way to the refectory, which I found to be a noble room with a southern aspect, set out with long tables where many of the staff were already seated, and in spite of the tempting meal set before them, were already engaged either in earnest conversation or disputation, and my guide explained to me that the rule of the house was that the members of the staff, with himself, took their meals together, as in this way they could discuss questions and difficulties without trenching on the time devoted to their official duties. "An excellent plan," I said, "and I suppose you preside?" "No," he replied, "I just take my place here or there among the members of my staff, and I find it does not in any way interfere with discipline to be on the friendliest terms with even the humblest, and encourage them to bring all their difficulties before me. I often find that I get valuable suggestions from even the youngest. Now sit down," said he, "and 'partake' of a good breakfast." In spite of the shock I suffered at hearing him use the vile verb, I accepted his invitation. "For," said he, "you will want all your strength before the day is out if you are to see everything." (Later I discovered an explanation, if not an excuse, for my learned friend's language, for in the course of our talk I found he was a regular and diligent reader of the *Daily Mail*.) So I "partook" of a very excellent breakfast, and announced myself ready to follow him to the bitter end.

Leaving the refectory he led me downstairs to what he called the upper basement, the lower basement being reserved for machinery. "Machinery!" I said; "what do you want with machinery in a library?" "We have our engines for various purposes, for working printing presses, lifts, and anything else requiring power," and with that he led me into the compositors' room, which, though in the basement, was a large, well-lighted, and well-ventilated

apartment, where I found compositors busy filling up forms from written copies of catalogue slips.

"We find it much cheaper to print our catalogue cards, and an economy of time for our readers and searchers. In the usual card catalogues there is one principal entry, which contains the full description of a book, while the numerous cross-references are limited to 'See so and so.' We print as many copies of the principal entry as we think necessary, and then write a short heading on each of the cards to be distributed through the rest of the alphabet for cross-reference, so that the searcher, on finding any cross-reference, gets all necessary details. Had these cards to be sent out to a printer much time would be lost, whereas by the 'Osler' method an hour after a book is received cards with full descriptions can be placed in our catalogue. When the cards for the day are printed off, *clichés* of them are made and stored away until the time comes when they can be used for printing a great General Catalogue."

In the next apartment were the printing machines, and I asked whether their noise did not disturb the readers upstairs. "No," said my guide; "we have safeguarded against that, for the architects have interposed double floors packed so that not the slightest sound is heard but occasionally a slight vibration."

From there he led me to the bindery. "No book ever leaves the house except to go to a reader. 'A stitch in time saves nine' is nowhere so true as in a library, where a loose leaf or cover neglected often means the destruction of the book, so whenever a book shows the slightest signs of disrepair, it is sent down here at once and dealt with by skilled workmen, who know how to repair a book without spoiling it. In the next room the actual binding work is done by men specially trained in binding books *for library use*—a very different art from that of the ordinary trade binder. I should allow no one to pass as a qualified librarian who had not a practical knowledge of binding. I don't mean to say that he should be skilled enough to do the work himself, but he should know how instantly to detect bad workmanship. There is no reason why a man should not be a scholar and yet have a practical knowledge of the arts connected with his work. He may be a student of Lamb and know him by heart, and yet should know better than to bind his books in sheepskin and—while properly despising 'rogues in buckram'—

should know how excellent a covering is buckram for what we call 'upper shelf books,' i.e., books which we must have but are rarely referred to.

"By doing all this work inside we practically enrich our library, for is it not an impoverishment to have books away at the binder's for sometimes three months? And here in the case of a single copy of a book which may be in the bindery, if it is important for our reader to see it at once, he is allowed to look through the book, which as a rule serves his turn. If he must have it for a longer time, the binder's slip is marked 'urgent,' and rarely has he to wait for it more than three days."

I noticed an extraordinary number of tubes attached to the upper part of the walls and almost covering the ceiling of the basement, some of them were about 2 or 3 inches in diameter, others much larger, which my guide explained were pneumatic tubes for all kinds of purposes. The smallest ones were for the passage of messages from one department to another. These messages were enclosed in a small leathern cylinder, literally flashed from one end of the building to the other, and so contrived that they were released almost at the desk of the official they were intended for. The larger ones were used for books up to a limited size. By this means instead of waiting for an hour or more for a book, a reader could be sitting down before his book within five minutes of entering the building.

Beyond the bindery, and next to the engine room, there was an electric plant. "We believe in having two strings to our bow in every important essential, and cannot risk a breakdown of the municipal supply, so we produce our own current, and find it economical, while we have an alternative connection with the city plant, to be turned on only if our own breaks down. Here we have the power required for every other purpose, including warming, for we decided not to run the risk, however remote, of our galleries and shelves being flooded by bursting water or steam pipes, and the radiators are heated by electricity, while in the staff offices the cheerier electric stove is installed. Current for everything requiring power is provided here."

I expressed admiration but ventured a criticism. "You appear to have taken every precaution against fire, and yet some of the

worst fires have taken place in so-called fireproof buildings, for even if there are no open fires in a building, an accidental spark from the electric plant, or a short circuit, encouraged by such excellent fuel as furniture, wooden shelves, etc., soon provides a bonfire."

My guide smiled and said: "I am glad you mentioned that; otherwise I might have forgotten to mention that our furniture and carpets are fireproof—a very simple and inexpensive process—and you will see why we do not dread fire."

As we turned toward the upper regions I observed a large trolley full of books emerging from one of the lift doors, and I remarked, "I suppose these are going to the bindery." "Oh, dear me, no! They don't need binding, they are going to the dusting room." "Dusting room!" I exclaimed; "what do you mean?" "I will show you. In discussing the plans for our building with our great Chief, he said, 'Can you not contrive some way of getting rid of that infernal nuisance, the annual closing down of the library for cleaning?' It practically means that in most libraries it is useless for sometimes two months in the year, and to me it has always seemed that the 'cleaning' would be honestly defined as 'shifting the dirt from one place to another.'

"Well, we took the matter 'into avizandum,' as our friends in the north say, and this is the result. We don't intend ever to close the library for cleaning. The cleaning goes on day by day and every day, in regular rotation. The books are lifted gently (so as not to disturb the dust) from the shelves and placed on one of these noiseless rubber-wheeled trolleys, conveyed to a lift and brought down here by the cleaning staff, while others during their absence wipe down the shelves with a preparation which holds the dust and leaves the shelf perfectly clean. Come into the dusting room."

We followed the trolley and I found myself walking nearly ankle-deep in moist sawdust. The expert cleaners seized the books one at a time, and holding the fore edges tightly, sprinkled the tops with clean damp sawdust, which immediately licked up the dust and was thrown on the ground, when the book was then carefully dusted clean with cloths containing the same preparation, which not only cleaned them, but I was assured acted as a preservative to the binding. When all were clean they were restored to their place on the trolley and carried back to the shelves.

We accompanied the trolley on the lift and were carried to the main library room, a magnificent, well-lighted apartment shelved all round the walls and with projecting cases in the old-fashioned style, forming little bays to give nervous readers an opportunity of doing their work in modified isolation. The shelving seemed of oak, but my guide asked me to examine it more closely, and I found that both shelves and uprights were formed of steel, so artistically enamelled that unless actually handled they appeared to be of fine-grained oak.

My guide went to one of the bays, and, putting his hands under one of the shelves, lifted it and the books together and laid it on the reading table, and then showed me how, by a cunning invention, the shelves, while quite safely fixed in position, could, by touching a couple of springs at the ends, be instantly released and thus enabled space to be economised to the minutest degree. The tables were of the same material as the shelves, and the oaken chairs, designed for comfort but yet artistically, were, as he explained to me, absolutely fireproof.

My guide explained that this room, called the general, or main library, was the largest, and for the general reader, the favourite room. The other rooms, to which he proposed to lead me presently, were for special study, for the use of readers who were engaged on research, or themselves writing books, and for whom it was desirable to have a certain amount of seclusion, and their books kept together.

The general lighting was by reflected light thrown by powerful electric lamps against the white ceiling, by which a delightfully equal light diffused through every corner of the room, while on each reading table I saw there was a separate shaded electric lamp provided with current through a cunning attachment to the pedestal.

"How do you classify your books?" I asked. "We don't classify them. You can't classify a medical library without doing more harm than good. If all medical books were monographs, it could be done, and probably would be useful; but when you remember under how many subjects medical books might be looked for, you will recognize that to classify them under one subject would be hiding them in all the others. Therefore, we find that for practical purposes, both as regards economy of space and quickness of service, it is better to shelve the books chronologically and according to size. This means

that our library begins with the earliest books, which are in the remoter parts of the library, and so we march down through the ages, and the books published during the last ten years are the most accessible, and the book last received is the last one on the shelves. We depend for our classification on the catalogue in which a reference should be found to any particular book, under every subject with which it deals." I noticed on the larger tables bulky volumes that looked like atlases, and on turning them over found they were filled with original drawings of all kinds—pathological, anatomical, surgical, and bacteriological. "Ah," said my guide, "that is a feature we are rather proud of. Beautiful and valuable drawings are constantly being made for authors, to illustrate their books and papers published in Transactions, etc., and for the most part, these were destroyed, or at least wasted. Some authors might keep them for a while, but sooner or later they found their way to the dust bin. Now, we have a clerk who, as soon as any particularly good drawing is published, writes to the author and begs him to let us have the original for preservation and display. They are then mounted in these albums with a reference to the paper or book for which they were prepared, and are duly entered in our index. No reproduction of a good drawing can ever equal the original, if only for the reason that, as a rule, they have necessarily to be reduced; and we find our collection immensely appreciated and in constant use. You will see that there is some attempt at classification in these albums. One album will be devoted to drawings of the surgery or anatomy of the thorax, another to the bacteriology of a particular disease, and so on. Sometimes the author will not part with his drawings, and in that case we get the loan of them and make full-size permanent photographs of them to mount in our albums. When our photographer is not busy with such work, he fills in his time by photographing from perfect copies illustrations and sometimes title pages to enable us to make good imperfect copies of our rarer treasures; and we have even been able in this way to produce wonderfully good complete copies of unique books and manuscripts, which can only be found in older libraries.

"What are those type-written folios I see displayed on that desk?" "Let us look at them," said the Chief, "as that, too, is a feature we are rather proud of. In a library like this, men are con-

stantly looking up references in connection with their own work, compiling bibliographies, so essential an adjunct to any good medical book. Formerly, this work done, we saw the last of it when their sheets were taken away for the printer; and so we offered all such workers to present them with a fair typed copy of their work on condition that they allowed us to keep a duplicate, and in this way we have secured many hundreds of valuable bibliographies, which are preserved here for the use of others."

We walked on to the adjoining room, equally lofty and equally handsome but smaller, but this I found to be a reference library, from which, my guide explained, no book was ever allowed to be removed except to the bindery. "Not under any circumstances," he said; "for we regard it as essential that there should be a copy of every important book *always available*. In the practice of medicine and surgery, 'next week' or even 'to-morrow' should never be heard in a library. Where life or human suffering is the price to be paid for delay, there must be none, and therefore a sudden demand for any book likely to be required must be instantly answered.

"Without our reference library another of our departments would be handicapped if not impossible. One of the items in Osler's prescription ran, 'Make the library as useful to the worker in Timbuctoo and Tierra del Fuego as to the man who lives round the corner.' I wrote him, 'Excellent idea, but how?' He wired back, 'Oh, *you* know—quite simple—I'm busy.'

"So we had to work it out. We invite our readers abroad and at a distance to keep us informed as to their lines of work or research. Their names are registered and classified—and every month we send them a 'Bulletin' containing references and abstracts of all that has been published on their subject during the previous month. If they want more, they write to the head of our Abstracting Department, and copies and abstracts of articles in books or journals (translated when necessary) are despatched without delay. One of our correspondents lately wrote, in the preface of an epoch-marking book which he had written on the slopes of the Andes, that our help had made it easier for him than if he had been living in London, for he had been saved the time he would have had to spend in making his own researches in the library!"

"But," I said, "all this must cost a fabulous amount. The

running expenses alone must equal those of a township. You must have an enormous number of members who pay a high subscription." "Members," he answered, almost indignantly, "our members, as you call them, include every qualified man and woman throughout the civilised world. Once on a Register a man or a woman is entitled to the best we can do for them without any subscription." "Ah, you are a State Department?" "No, we are absolutely untrammelled. I thought you knew the origin of the scheme. You remember that twenty years ago Osler celebrated his seventieth birthday and now, although by the calendar, ninety, he seems determined to prove that a man is not too old at a hundred. The whole civilised world, on the approach of his seventieth birthday, wanted to celebrate it in a way really worthy of their hero, and many meetings and long discussions were held on the best way of doing it. Carnefeller got to hear of it and summoned the testimonial committee to meet him; brushed all their suggestions on one side and said, 'The only sane way of celebrating Osler's biological palinode is by erecting a library which will realise all his ideals, and if you will carry it out I will provide the dollars,' and here he handed a cheque to the chairman and left us. On examining it we found the cheque was signed in blank, and in the course of a few minutes it was filled up with such a sum as would cover the most ambitious scheme, with a sufficient margin for a liberal endowment and, just in case of accidents, promptly banked."

"The *body* is wonderful," I said, "and your mechanical part seems to be as perfect as could be devised. But what about the *soul*—the *intellect*, of this wonderful *body?*" "I was hoping you would come to that," said my guide. "I am the Chief, but I don't pretend to be either the soul or the intellect of such an institution as this. The Chief should be before all things an administrator and a business man, or the whole institution will suffer. We have in all, at present, twelve librarians, each of whom is supreme in his own department, and I verily believe each is the greatest living authority on the subject he deals with." "But how can you get men of such attainments to accept such positions? For while I am sure that the matter of salaries is dealt with as liberally as everything else in this wonderful institution, men of such attainments would probably be earning princely incomes by the practice of their profession."

"No, you are quite wrong. You will find in every profession men who are by temperament students rather than practitioners, and who would rather work for a modest competence in extending their knowledge than in the practice of their profession, and this is notably so in that of Medicine. And so we have here, for example, a man who has, perhaps, a better knowledge of anatomy than all the professors put together, but he is happier here adding to and administering our anatomical collection, than he would be if he held the most important professorship. He has no faculty for teaching, and knows it; but raise any abstruse point in anatomy with him, and he will at once, without consulting any index or catalogue, place before you the answer to your question. It is the same with our surgical librarian. When he inadvertently removed the second kidney, leaving an overlooked forceps in its place, he decided that the practice of surgery was not his forte, and his love for and wide knowledge of the literature of the subject brought him to us. And so it is with each of the others. They have not exactly a free hand in their departments, for some of them would spend all our available income on their own department; but they come to me with their lists of desiderata and I decide, having in view the necessity of a fair balance between one department and another. We are in constant communication, in addition to the practice of taking our meals together in the refectory. And each has his own room, connected by telephone with mine. We make great use of the telephone." At this moment, I saw one of the assistants on a high ladder perilously balancing some heavy volumes, and before I realised the danger, boy, books, and ladder fell with a crash towards me.—When I came to myself, I heard the telephone ringing, started up, and found I was in my own chair by my own fireside, and rushed to the telephone. "Hello! Is that Mayfair 3271?" "No, wrong number!"

THE EDUCATION OF GRADUATES

By Sir Andrew Macphail, Kt., B.A., M.D., M.R.C.S. (Eng.), L.R.C.P. (Lond.), F.R.S. (Canada),

Professor of the History of Medicine, McGill University, Montreal

MEDICINE is the only profession which shows any concern for the further education of its graduates. Upon a given day the graduate may profess that he has acquired the mystery, but no one believes him. There is a great gulf fixed between knowing a thing and professing to know it, and a still wider gulf between the knowing and the doing of it. Study of medicine must continue so long as life endures.

Medicine is a profession with an immemorial tradition of service, to be rendered freely to humanity, with a single eye and a pure intention. The votary is set apart, empalisaded, or crucified to the world, as one might affirm with textual truth. He testifies not that he has all the knowledge of the masters, but that he has entered into their spirit, and has the beginning of wisdom.

The entrant upon this career also signifies that he brought with him to the schools a mind, and that something was done to that mind whilst he remained at school; that, in short, his mind was educated up to such a point as the original material would permit; but always remembering the dogma which underlies the fable of the silken purse and the sow's ear.

This process of education is carried on by the senses. Eyes are taught to see, ears to hear. Events are observed, and some effort is made to understand their sequence, connexion, and results. Medicine in the case of each student is thus freed from its old habiliments of witchcraft, magic, and sorcery; it is become scientific, and in his own time the student lives through the whole history of the art.

If every graduate brought such a trained mind to his advanced studies, the problem before the teacher of graduates would be easy. He would continue an education which had begun long years before,

and raise it to a higher point. On the other hand, if the mind is not receptive, discriminating, able to assimilate or reject, it will not integrate the new learning into itself; and what should make for strength is become a useless burden. Graduate study may then be worse than useless if it clogs a dulled and uneducated intelligence.

It is quite true that these considerations apply with equal force to the undergraduate. He may have entered into the new world of medicine with a mind unaccustomed to intellectual processes, or brutalised by a long routine which goes by the name of secondary education. It must, however, be placed to the credit of any system of study that, whilst it allows many aspirants to proceed, it destroys the ambition of others, and directs them into more lowly paths. Even a bad system, if not too hardly pressed, is better than none at all.

And working still further back, we are bound to notice preliminary education, which is the first step towards entrance into any profession or any trade; and there we shall discover the source of all our evils, industrial as well as professional. These evils in turn have arisen out of a civilisation which has become detached from the soil, and is now in all essentials a slave society in which any little Spartacus may seize control.

It is a condition of life that the experience of parents shall be transmitted to their young. The she-wolf teaches wolfing to her pups, and the bird flying to her fledglings. Domestic animals alone are allowed to grow up in ignorance. Without tradition, without art or craft, the yoke of servitude is the more securely fastened upon them.

Within the time of the present generation the young of the human species has fallen to the level of the domestic animals. They are taught nothing. They are segregated from older persons from whom they might learn. They are immured in a building. To quiet their minds and quell their spirit they are given a series of tasks which are all one task—namely, to regard certain emblems fixedly. In time these black emblems upon a white page combine themselves into categories which are known as words; and these in turn are considered to be the same as things.

We have been astray in our education. We have been equally wrong in our science. We have mistaken facts for truth, and placed

all truths in the same category, estimating the number of persons and things in a country as equal in importance to the truth, "that the kingdom is within you"—that, in short, physical facts are identical with moral truths, that research in a laboratory is the same as research in the mind. We are prone to think ourselves much wiser than our fathers, but the veracity of angles was known to Euclid, and the veracity of life to the Hebrew prophets.

Even in matters of pure fact the ancients were not so ignorant as we are fain to suppose. Most of our scientific discoveries are nothing more than explanations of world-old experience. The cave mother observed that her offspring must eat animal fats and raw vegetables if they were to have sound teeth and hardy bones. We have allowed teeth and bones to decay whilst we were inventing the term "vitamines." There are persons yet living who remember the days when the child of humble parents was at first suckled, and later allowed to gnaw a piece of carrot or turnip; to suck an apple, orange, or lemon; or even chew upon a piece of muslin containing a morsel of raw meat, and fastened to the waist by a string to prevent its being swallowed. The same child was permitted to come to table and complete its dietary by snatching a wholesome piece from its mother's plate; whilst the child of the rich was segregated in a nursery and starved upon a scientific food.

There is now some hope that we shall revert to the earlier practice, since the Royal Society has allotted a Royal Medal for the discovery—to employ the modern jargon that when, instead of the eighteen different amino-acids composing the protein, five only are administered, death rapidly ensues if those five be selected from the simpler aliphatic components—for example, leucine, valine, alanine, glycine, and glutamic acid; but that, on the other hand, nutrition and life are satisfactorily maintained, at least for a considerable period, if the five amino-acids given be chosen from the more complex types, such as tyrosine, tryptophane, histidine, lysine, and cystine, which experiment has shown to lie outside the range of the synthetic power of the animal body.

Astonished by the complexity of our discoveries, we are blind to the larger issues of life; but it is the fate of every art and of every school to think that it has attained to finality. Pneumonia was definitely mastered in 1805. In 1860 Erichsen asserted that surgery

had attained its fulfilment; and no surgeons were ever so vociferous as those who declared in 1914 that they had arrived at a perfection of technique. When put to the test of war they discovered that they had merely attained to a mastery of wounds which they created with their own tools under conditions selected by themselves. It was more than two years before they had devised a surgery suitable for war.

It was thought that all the fields of medicine had been at least surveyed; and yet trench fever came upon us like a new calamity. As long ago as 1597 an epidemic fell upon the world. Calenus described it as *ob occulti cœli influentia*. We call it influenza, and are pleased with our perspicacity. We have isolated from children's diseases, and these diseases fall upon armies of adults with the force of a new plague.

If, now, I have left the subject no clearer than I found it, I have, I trust, shown how complicated it is—that all education is one, that a pernicious beginning works its evil through the secondary school, the university, the professional school, and the graduate course. But things are what they are, and those who have to do with advanced medical education must deal with conditions as they find them.

English medicine has always proceeded upon the assumption that new discoveries can be made only by following out old paths; and rarely has it entered upon those paths which lead nowhere but into the desert of barren speculation. Medicine is an art founded upon observation, with experience alone for its guide—observation, that is, with the human eye of the complete patient, and not of parts of him in the form of a slide under a microscope.

When medicine forsakes the patient it becomes futile. And this patient must be regarded as he is, in the circumstances in which he chooses, or is bound, to display himself. When medicine leaves the bedside it is lost. The post-mortem table also is a kind of bed, a κλίνη, and its teaching clinical. To the bedside the Father brought medicine, and there he left it. With the cold Greek precision and serene impartiality, which the English have inherited, he recorded what he saw, and his case reports remained unmatched for lucidity until the time of our own Sydenham.

Medicine is a way of life, and the prospective practitioner is the

best judge of how far and how fast he can go. He knows his own capacity and feels the bounds of his ambition. He has a safe instinct either for the village practice or the consultant's room. Breeding, training, position, all impose their limits. The doctrine that any man can do anything is quite new and quite false. The first business of the teacher is to provide practitioners, not to create scientists, and the two are by no means identical. The truth is that the function of a medical school is not in itself intellectual nor scientific. Its final work is to create a reasonable nature and an honest mind.

No student can learn even a little of everything. A student who has not developed an instinct for following what is true and turning aside from what is false has learned nothing. Even scientific medicine has always been prone to lose itself by following after false gods. It has always found the true path by returning to the human body. Of all new schools anatomy has ever been the root, not the anatomy of the oyster or the frog, but the structure of the human frame. That is the one safe preliminary scientific study. Anatomy, like geometry, can be learned by sheer force of industry. Its truth is apparent in itself, and does not depend upon authority. Of students who in the beginning are systematically bewildered by biological subtleties few ever afterwards find their way.

English medicine has always proceeded upon the belief that every student could learn something, and it provided for every student as much as he could learn. It also recognised that for the average practice a definite degree of knowledge sufficed if only the mind were open and the spirit honest. A man must judge for himself how much he is able and willing to learn. Accordingly, certain standards were set, or, rather, one standard was set with successive marks upon it, against which a student was free to measure himself.

In the United Kingdom there were in my time, and I understand it is so yet, twenty-four of these marks, and a candidate might choose any one as his measure of growth. Having attained to one he might aspire to another until his full stature was reached. Up to a certain point the teaching was identical. It became more special as the student advanced from licentiate to member, from member to fellow, or doctor. In the clinics at least all candidates met together, and each took as much as he could master. The teacher soon distinguished between the receptacles, and the overflow from

one was received by the others. All teaching then was graduate teaching.

The history of medicine did not end with the Renascence. It has ever since been, and is now, in progress. It is governed by causes which are immutable. In medicine, as in all other arts, life and death go hand in hand. When it appears to flourish most it has already begun the slow gradation of decay. In the backward abysm of time one discerns certain glowing points: the approach and descent are lost in the void of history.

Up to the Renascence the whole story can be told in one sentence. Hippocrates stood midway between that event and the earliest Egyptian, with a period of 1700 years behind and before him: from the twin roots of anatomy and physiology medicine arose in Alexandria; it divided into three branches—dogmatic, empiric, methodic, to which Galen, Sextus, and Soranus have affixed their respective names: it took refuge amongst the Saracens, and was next discovered in the school of Salerno, where it remained in Græco-Arabic guise until it was united again with its great Greek original. In that long period medicine had wandered from Cos to Alexandria, to Rome, to Gondisapor, to Salerno, and only met with science, as now we know it, in the person of our own Harvey; and the two grew into one in the line of Bichat and Laënnec, as Dr. Whittington has so acutely observed.

The subsequent story is modern; but, ancient or modern, medicine has always been a part of life, no better, no worse, and not different. When deep darkness settled down upon humanity medicine was equally engulphed. We ourselves have lived through one of these periods of efflorescence, and did not know it. The signs now are that this time of flowering is at an end. None can say how long the seeds will lie dormant or what the resurgence will be.

When the medical history of our own time comes to be written the point most clearly observed will be the laboratory. Uniformity of teaching will be disclosed as the guiding principle of our education, based upon the predominance of the machine as the motive of industrial life.

Eight years ago a voluntary appraisement of medical institutions —as if they were iron mills—was undertaken by an American device, known as the Carnegie Foundation for the Advancement of Teach-

ing. What turned out in effect to be a "black list" was prepared. This list in the hands of a powerful rival was a deadly weapon, and it was used with effect; but with the elimination of the feebler schools much sincere teaching also perished.

No one dissented from the accuracy of the verdict upon the principles formulated and the evidence adduced; but the principles themselves were challenged, and the evidence was impugned on the ground of inadequacy. The report dealt with externals, material equipment, and uniformity was glorified.

In these eight years, and especially in the last four, we have learned much, and there is at the moment a delicious irony in reading Mr. Flexner's report. We can now accept with some complacence his charge against the English consultant, that "scientific distinction is a becoming decoration; it is not the breath of his nostrils." We, too, like Mr. Flexner, have been amazed at "the speed with which a novel standpoint travels over Germany"; but we are now less enamoured of travelling standpoints and more content with our own, which remain fixed. "This quick apprehension and incorporation of 'demonstrated truth' is responsible," Mr. Flexner has "repeatedly pointed out," for "the uniformity of the scientific institutes in respect to type, organisation, and ideal."

We may well be forgiven if we do not now share his ecstasy in contemplating a perfect uniformity. Diversity is the law at least of English life, and at its peril the whole earth becomes of one language and one speech. From this dead level men begin to erect anew a tower of bricks and slime, whose top is intended to reach unto heaven, so that nothing can be restrained which they imagined to do. His giantship of uniformity is going somewhat crestfallen in these days, walking with less unconscionable strides. English medicine and English life may now take leave to be less apologetic about its existence in the world.

There were physicians in the world before Hippocrates, and there were teachers of medicine in England before the scientist immured himself in his laboratory: no one but an ignorant and Chauvinistic fool will decry and deride what is done outside of his own borders, or fail to give credit where credit is due. There is a deeper folly in following false gods just because they are alien. Moloch and Juggernaut we have seen face to face, and we have not

knelt down or taken to flight. It is not by mere chance that Paracelsus, the master quack of history, had for proper name Von Hohenheim; but it was a strange accident by which his first name happened to be "Bombast."

English medicine in the last thirty years has lost its pre-eminence merely because it stood still, declining to follow in the false path which was marked out by an alien school. This path with its signs, "efficiency," "progress," "science," has demonstrated itself to have been false, and English medicine may now resume its march by way of observation and contact with the reality of disease.

The genius of English medicine has always lain in its power to observe cases. Disease is a thing in itself, and can be recognised as easily as flowers of the field or the faces of friends when these are seen often enough. London is the place of all the world where cases may be seen. No other can compete. Laboratories may exist in any corner, and research can be carried on in the dark. Provincial towns have their own sphere, as the German towns had. They may well continue to be the resort of specialists, but London will stand unrivalled as the centre where cases can be seen. From cases all practitioners can learn something, and the few can learn much.

But medicine is not all of Medicine. Craft and art have their place; and of graduate medicine hand work leading to technical skill is the principal part. To observe is not everything; to do is its fellow and consequence. The graduate is not now content with looking over the shoulder of another: he must work with his own hands. Of all men who profess an art or craft the recent graduate is the most ignorant, however learned in science he may be—more untrained than a nurse, more incompetent than a medical orderly. In this chasm lies the main use and success of the modern graduate school.

Men are no longer content to "walk." They demand a place where they can stand still, or sit down, to work with their own hands. This was the valuable part of the German discovery. The Vienna clinic in laryngology owed its fame to that old woman, Frau Gaille, who upon her own person taught the graduate the use of his tools. The London teacher may teach with the tongue of an angel, and yet be ineffectual unless he provide means for acquiring a handicraft as the old practitioner provided for his apprentice.

English medicine lost its pre-eminence merely because it declined to follow the fashion of the day. That fashion has passed with the nation from which it sprung, and the laboratory is assuming its former place as the adjunct and not the master of the ward. English medicine will then come into its own, and the clinical teacher will once more be the thing. There are men yet living who remember the great days of Wilkes (1911), Paget (1899), Jenner (1898), Bowman (1892), Gull (1890), Fagge (1883), Watson (1882), Murchison (1879), Hilton (1878); and the tradition is still alive of Brodie (1862), Addison (1860), and of Bright (1858). So modern seem Hutchinson, Pavy, Matthews-Duncan, and Hughlings Jackson, that, though they be long dead, they yet speak to us.

The succession in English medicine has never failed, and will not fail even if at the moment it appears to be in abeyance. The history of physiology may be cited as proof. It is the simplest and most obvious. The first to give formal lectures on histology and physiology in England was William Sharpey at University College in 1836, and he continued to lecture until 1874. He begat Burdon-Sanderson, who succeeded him and then went to Oxford; Michael Foster, who founded the Cambridge school; Gotch, who succeeded Sanderson at Oxford; Schafer, who succeeded Sanderson at University College and is now in Edinburgh. These men in turn begat the present school of English physiologists.

Sharpey taught physiology by exposition and discussion, by inciting men to observe the natural phenomena rather than by experiment, although he did not neglect it. To him physiology was one of the humanities. The modes in which life was manifested and maintained were, he taught, matters that should interest every intelligent man, and were of particular concern to those who aspired to be physicians. By him the best minds were directed to study disease as a derangement of function; and, directly or indirectly, all the English physicians in the mid fifty years of the nineteenth century were influenced by his teaching.

At this time the biological sciences were concerned almost exclusively with observation. The names of Owen, Hooker, Lyell, and Darwin prove it. The physicians belonged to the time, and they too were observers. In teaching they used the method of exclusion. Their diagnosis in the ultimate resort rested on post-mortem

observation, and when the case was fatal they were nearly always right, or right in part. As William Jenner once said, "I usually find what I expect to find, but nearly always more than I expect."

In our own time this science of observation has fallen into decay, and physiology itself has been affected, due, as the Medical Research Committee as late as September 30, 1918, reports, to a defect in the system of education, which has allowed the physiologist to remain too much in academic retreat and the clinician too far from the laboratory and its methods.

Scientific research in itself will not make a medical school, graduate or undergraduate; but a medical school without research is like a ship without a compass. Yet even with this useful instrument the course is never made in the direction to which the needle points. The course is shaped, and the compass keeps it true. A school without guidance of the scientific spirit towards the end that cannot yet be seen will quickly miss the things that should, and can, be seen. The lonely worker in the laboratory, who deals with truth in the abstract, is monitor of those who work publicly in the wards. He is looked upon with respect and fear. He is to the school what the eye of God is to the world.

Those who by taking thought would institute a formal system of graduate instruction in London would do well to remind themselves that such attempts in the past either ended in failure or had at most a partial success. The experience of the London Medical College and Polyclinic, of the London School of Clinical Medicine, of the North-West London Post-Graduate College, and of the London Post-Graduate Association will be remembered as proofs.

But if these experiments do not encourage, they need not deter. They had their uses. Down to the year 1884 the fortnightly meetings of the Pathological Society in the old hall in Berners Street were crowded with the keenest men in London, and drew an audience from the provinces; but when bacteriology, the infinitely little, and experimental medicine became dominant they faded away. Before the year 1852 there was a society which demonstrated What to Observe at the Bedside; but it dissolved when Argyll Robertson observed without its aid the somewhat obvious phenomenon which bears his name. Nothing is permanent.

Medicine being a part of life has been for the past four years a part of war, and it is as such that it is now known to several millions of men. Medicine has come out of the college and the consulting-room into the field, not with trailing robe, but in soldier's garb, as a hardy, humble, and faithful servant. To these millions of men medicine is now identified with the medical corporal and the stretcher-bearer, from whom they never failed to receive quick and efficient aid.

These millions will in future look to medicine for service of the humbler kind, which will in turn remind medicine of the humble origin from which it is sprung. This should be a warning to those who would make of medical study an over-elaborate procedure, a too scientific and dignified pursuit. It may even come about that perhaps after all Harley Street will not be considered the only delectable abode in the world, and that the dressing station of the field will take its place in civil life, where for a humble sixpence can be obtained relief which is now laboriously sought at an expense of two guineas and much time.

Medicine in London is at a standstill because men are waiting for the waters of the University to be troubled. They have been waiting for forty years, waiting for the machine, and neglecting the man. It is not without meaning that London has never been a medical school, but a congeries of schools, competitors for students, without any common meeting ground, or any common standard of teaching or attainment, except in so far as the Royal College of Physicians and the Royal College of Surgeons, which give diplomas, determine a standard by their requirements for examination. The physicians are not materially different, although the College of Physicians is governed by the whole body of Fellows meeting together; whereas the College of Surgeons is governed by a small council elected by the Fellows of the College. Even when London was at its best there was no central body with authority and resource adequate to warrant the task of attempting to co-ordinate teaching and research. The University of London has long been a national or imperial university without a teaching staff; and although the medical schools are called schools of the university, they are yet independent bodies, and not one-fifth of the students are undergraduates of the university.

Some organisation, of course, is necessary for graduate as well as for undergraduate teaching. The two are one. The Royal Commission on University Education in London in 1913 recommended as good a means as any—namely, that three hospitals with medical schools attached should be established as constituent colleges in medicine of the University of London as reorganised; that in each of these medical colleges there should be professorial chairs in the three main divisions of medicine, surgery, and gynæcology, with associate professors.

The kind of organisation known as the "hospital unit" appeared to the Commission to be well fitted for attaining this end. In the words of their report, it consists of a professor with the control of wards; an out-patient department; assistants nominated by the professor with a view to completing his own knowledge and affording him the special assistance he requires to carry on research in the direction in which he is interested; and finally, laboratory accommodation in close proximity to the wards, not only for the service of the wards and the examinations and procedures connected with the diagnosis and treatment of the cases, but also for the purpose of research.

Nothing could be more simple or more complete. It is simply a question, in the words of the report, of appointing a university professor and arranging that his department shall be so organised that he will be able to do his work. A professor of literature or history must have his library; a professor of chemistry must have his laboratory and assistants. A professor of medicine requires the organisation of the hospital unit, provided he is to carry out his threefold duty of curing the sick, studying the problems of disease, and not only training his students in the technique of their art, but giving them university instruction in the science of their profession.

At a later date, after medical colleges of sufficient size and number to provide for all the university medical students in London had been established, there would, the Commission thought, be no objection to organising a hospital of smaller size as a post-graduate school for the reception, partly of graduates from abroad, and partly of students from the other university hospitals who desired to pursue their studies.

This last is a disputable doctrine; for, let it be reiterated, graduate and undergraduate teaching are one. It has indeed already been disputed in the Memorandum on Medical Education in England, issued in the autumn of 1918 by the Board of Education. This Memorandum, by Sir George Newman, the chief medical officer of the Board, tells impartially the good and the bad of the existing system, but for the present purpose it will be sufficient to notice that in it graduate instruction is reckoned as part of a complete medical curriculum. Some arrangement is demanded by which "all students shall receive special post-graduate training of one form or another before embarking on general practice, preferably in resident clinical appointments in general or special hospitals, Poor Law infirmaries, and dispensaries." This is the English ideal. With it is linked the injunction that some arrangement must be made by which "all practitioners shall find facilities available for periodically bringing their knowledge and practice up to date." Again we are told that post-graduate instruction must form an integral part of the curriculum of the ordinary medical school, with extension to special subjects in special schools. Finally we have a picture of an imperial graduate-teaching scheme in England for graduates from the Dominions and foreign countries to serve as a teaching centre, to advise appropriate courses of study, and to facilitate their provision.

No institution ever reforms itself from within. Men are too loyal to each other, too closely bound by the bonds of interest and affection. If such a problem presented itself to the Army, it would be solved "from above" in four days. Sir Thomas Goodwin, Sir Charles Burtchaell, or Major-General Foster, according to the area involved, would detail an officer for the task. He would assign to each hospital the course for which it was most suitable, and he would see that it was carried on with joy. In this there is a hint for the Minister of Education, and for the London medical schools as well. What they will not do for themselves another may be found to do for them.

But lest something should be left unsaid, let it be affirmed that even in the idea "university" there is nothing sacrosanct. A university will not save unless it has the spirit and a willing mind. The good it does is done mainly by the prevention of evil. In its own turn it may develop the sectarianism of the school, make of three schools one, and in the professor lose the teacher.

Up to thirty years ago London was the medical centre to which all the world had resort. It lost that pre-eminence when the passion for teaching was destroyed by the appeal to mechanical experiment and the desire for uniformity. For more than thirty years earnest men have tortured themselves in the vain discovery of an alien method for the English mind. But the English mind would have none of it. Attend to the education of students, and the education of graduates will take care of itself—that was the final dogma of the Royal Commission on University Education.

London lost its pre-eminence in medicine because the breed of teachers died out, and the breed died out because it was not diversified and enriched by an allied strain. A medical school and hospital became a closed corporation, and men were promoted to teach merely because they were the oldest survivors of a system. There are in the world at any given moment very few teachers; for a teacher is an artist who transmutes, or mints, and sets in circulation, the ore which the scientist discovers, although in the rarest instances he himself may be artist and scientist too.

Teaching is the most precious of all gifts, and medicine without that aid perishes in all its branches. There is nothing more pitiable than the performance of a teacher who lacks the spirit. The performance is impious; the man is a charlatan; and the school where it is permitted is a mercenary school.

Upon those in London who are waiting, and upon those who are planning, it may be urged again that the Kingdom of Medicine also is within you. A school grows directly out of the mind of a man. Many years ago—nearly a hundred—there was a small school in a mean building in an obscure street of a small town. The root was there, transplanted from overseas like the Vine of Sibmah. At times it was gnawed to the earth, but it always grew again.

In the fulness of time there came a man. A man always does come in the fulness of time. He nourished and tended. By the winsomeness of his nature he won colleagues and students. A great school—great even amongst the schools of the world—was developed, and it remained great so long as it was resolved to lead and not to follow. Now, alas! it is without a Principal, and even the chairs of anatomy, physiology, and pathology are unfilled. This man was Sir William Osler, in whose honour I am privileged to make this piece of words.

From McGill he went to Philadelphia; to Baltimore; to Oxford. Wherever he went he left behind the perfect work of his hands, his mind, his heart.

Within the past four years something has happened. Whatever it was it did not happen by chance. It was due to the inexorable progress of events towards their appointed end. God does not pay every week, but at last He pays in full measure.

We have not yet begun to realise that the whole fabric of life is shaken and must come down to make way for the things that cannot for the present at least be shaken. We are like other blind Samsons, supporting for a little time upon our poor shoulders a fabric that is doomed, and groping about for materials of repair.

Such catastrophes are not new. Humanity will not dwell in the mountains where it belongs. It is always making excursions into the easy plains, and will not return until it is destroyed, leaving only a remnant to escape out of the overthrow.

These are no times for the making of formulas even in medicine. The best we can do is trust to the genius of the race. It will carry us through, as it has borne us down the tide of history these thousand years. It may well be that the day of the scientist even in medicine is over, seeing the calamity that science has brought upon us; and that men will forsake its pursuit, to frequent the shrine and consort with the saint; for magic, religion, and medicine have arisen out of the same protoplasm, as Sir William Osler himself has declared.

AN EARLY RECORD OF PERFORATING DUODENAL ULCER

By Archibald Malloch, M.D., Hamilton, Ont., Canada

Ecce sub oculis Domini res facta

A STUDY of early accounts of the symptoms and pathology of peptic ulcer serves to shew how painfully and slowly the true nature of a malady may be recognised. Hippocrates described the character of the vomitus and stools and from this named the disease "morbus niger." Although the diet recommended by Hippocrates in cases of ulcer of the stomach was very suitable, he had no very exact idea of the particular lesion. Friedrich Hoffmann of Halle (1660–1742) demonstrated the origin of the "atra bilis" in the stomach and recognised that the vomitus consisted largely of blood from the vessels of the stomach wall, these latter, in his opinion, being opened up by the action of the acid and biting juices. Morgagni (1682–1771) held that the lesion was of the nature of a gangrene of the stomach and did not think that there was a loss of blood. It was rather a poisoning of the blood, which affected the brain, as those suffering from the disease always died. He agreed closely with Hippocrates as to the peculiar nature of the "atra bilis." The term ulcus ventriculi was first employed by Johann Peter Frank (1745–1821) and the principles of treatment he laid down might almost stand to-day; absolute rest—*summa quies corporis imperanda;* the application of snow to the surface of the abdomen, a milk diet, and finally the internal use of serum lactis albuminatum as a styptic agent.

It is generally stated that Matthew Baillie (1761–1823) in 1793 was the first to give an accurate anatomical description of stomach ulcer. He described the shelving floor of the lesion and published very accurate and clear plates. Cruveillhier (1791–1874) described ulcus simplex chronicum for the first time, and in his "Anatomie Pathologique" spread abroad an exact knowledge of its pathology.

He withheld all medication and in a few words summed up the treatment, "le repos c'est la diète."

An old diary of Sir John Finch (1626–1682), a physician and diplomatist, gives an account of the very strange death in 1670 of "Madame," "Henriette-Anne d'Angleterre," daughter of Charles I, and of the post-mortem, which was performed upon the body. This case has become quite interesting in literature and history and Littré[1] quotes an account of the autopsy. A perforation was found in the middle and anterior part of the stomach, and although the peritoneal cavity contained a large amount of fluid and gas, and although this fluid was described as being oily, "grasse comme l'huile," it was not recognised that the perforation had occurred during life. France had yet to witness *l'Affaire des Poisons*, but foul play was suspected, as "Madame" had died nine hours after taking a glass of chicory water. The perforation, they thought, was made by a slip of the knife during the autopsy. It is evident, however, from the account given of the clinical picture of the case—and no doubts are left in our minds—that perforation of an ulcer had taken place before death and that the oil in the contents of the peritoneal cavity was none other than the castor oil, which had been given as a remedy!

One day in speaking to Dr. Charles Singer about the strange case of "Madame," I was told of the account given by Penada of a perforating duodenal ulcer. Penada's observations (apparently hitherto overlooked) form the subject of the present paper.

Jacopo Penada was born in Padua on December 11, 1748, received the degree of Doctor of Medicine at the University of Padua, and was for many years Prosector in the Anatomical School in that city. Stimulated by the researches in comparative anatomy of Antonio Scarpa, Vincenzo Malacarne, and Paolo Mascagni, such men as Rolando Cortesi, Ranzani, and Penada, in the late years of the eighteenth and the early years of the nineteenth centuries, carried out no mean work in anatomy and pathology. Indeed the results of their endeavours formed a basis for the extraordinary progress made since then in the more careful and minute histological observations of these sister sciences. Penada published in all some dozen works on a variety of subjects; on the structure

[1] "Médécine et Médécins," Paris, 1872.

of the heart and mechanism of the semilunar valves; on certain monstrosities; on vital statistics and rates of mortality in his native place; on a case of hydrophobia caused by the bite of an insect; on pellagra; on meteorological influences upon epidemics; on contagious ophthalmia, which he showed had spread in Italy even before the return of the Italian contingents of the French Army from Egypt; on epizootic diseases amongst cattle; and on the chemical nature of a calculus found in the centre of an external tumour. For one of his researches he was given the title of Honorary Professor of the University of Wilna by Emperor Alexander I of Russia. Penada died February 23, 1828. His style lacks clearness of expression and well-ordered arrangement of the matter, yet in seeking clarity he repeats himself *ad nauseam.*

Penada's account of the perforating ulcer of the duodenum is given in his book, "Saggio | D'Osservazioni, E Memorie | sopra Alcuni Casi Singolari | Riscontrati nell' Esercizio della Medicina, | e della Anatomia Pratica | dal dottor | Jacopo Penada M. F. | Socio Corrispondente della Reale | Accademia delle Scienze, | Lettere, ed Arti | Di Padova ec. ec. | In Padova MDCCXCIII | Per Approvazione | " This quarto volume of 146 pages contains nine chapters or "osservazioni," of which the third one, pages 33–56, is devoted to the case under discussion. Penada commences with a preamble of about two pages and then gives the history of the case.

"Domenico Miazzo of this city, about thirty-five years of age, of athletic habit, gifted with tremendous strength, a butcher by trade and a confirmed drinker, was accustomed to extremely hard work. Amongst other of his prodigies he made show of his invincible strength by carrying on his shoulder, hung from an enormous stick, the carcasses of as many as ten sheep or rams, called by us wethers ('castrati'), which together equal in weight more than four hundred Paduan pounds. In spite of continuous debauchery, he remained in a state of apparent good health up till about the 25th of May, 1791. From this time on, he began to complain of sharp pains in the region of the umbilicus and notably on the right side below the false ribs. These pains were very sharp and continuous and only a few moments after he had taken his necessary food, they caused him so much discomfort that he had to throw himself upon his bed, writhing in agony, until the severity of the pains had decreased somewhat, when he was able to stand on his feet and perform the labours of his accustomed and fatiguing trade. Although he was a great drinker,

he was accustomed to take little to eat, and on the days when he was attacked by those pains, he ate still less. On the contrary he drank more than usual, and this precisely because such pains in the intestines are wont to increase the thirst. Moreover, because he was guided by the false idea of flatulence in the intestinal tubes, he did not content himself with drinking, neat, of a rich full wine, but he went so far as to take spirits of wine and other spirituous liquors. However, the vital and animal functions of this individual did not seem to have greatly changed during these days and he occupied himself with his usual labours, neither did he ever spend an entire day in bed, although, as the days went by, the violent recurrent attacks became more frequent.

"And here, before going further, it is necessary to impress upon you that, during the whole course of the disease, the intestinal pains, although very severe and sharp, were not accompanied by vomiting of any kind, nor yet by any desire to vomit. Besides, it is to be noted that the movements of the bowels were quite natural and, although some pain accompanied the passage of the stools, yet these were not abnormal in amount nor abnormal in consistence. The presence of mucus or blood was not detected nor of any other analogous substance, which might point towards the existence of a morbid diarrhœa or dysentery or any noticeable alteration in the intestinal tube. Only three days before the death of this patient, i.e. on the 20th of June, 1791, the very severe pains, in the region indicated above, caused suppression of the stools and likewise of the urine, but, in spite of all this, he continued upon his feet until the morning of the 23rd of June, the last day of his life. In fact, on the morning of this day, in spite of having passed the preceding night midst a thousand violent attacks of pain, which griped the viscera, he got up out of bed and left his own house. When seven o'clock in the morning arrived (or as we should say, after the Italian fashion, eleven), our patient, making his way along the street feeling very weak and looking very wan, was suddenly overcome with so great a fainting fit that he was thought to be dead by those who rushed to help him. He was taken, until he should recover, to the house of one of his sisters near the place where he had fallen into a complete state of unconsciousness. In great anxiety they called me to visit this patient, who was lying at but a short distance from my own house.

"When I saw him he had already somewhat recovered from his fainting attack. When questioned, he complained of sharp pains in the region of the umbilicus, in the region of the cardia, of the pylorus, and of the neighbouring parts. But in the midst of such pains he did not have the slightest inclination to vomit. His pulse was feeble and irregular but there was no trace of fever. His face was pale and pinched. The eyes were

sunken in and the extremities cold to the touch. The muscles of the abdomen were tense and he was doubled up. The abdomen was somewhat swollen and more so on the right than on the left side. The urine and fæces had been suppressed for precisely three days. Besides this, he breathed with difficulty and was hiccoughing. All this was argument enough for the extreme severity of the disease and the evident danger in which the patient lay. It was difficult for me, with the information at my disposal, and considering all the circumstances, to state the exact nature of the colic in the present case. At once certain remedies suggested themselves to me as likely to bring some alleviation, if such were at all possible in so agonising a malady: doses of oil; local applications; clysters; and above all immediate spiritual succour. Greatly troubled in my mind, I determined to have the patient carried to our hospital, where, on the instant of his arrival, very many physicians came to his assistance; but all to no purpose. From hour to hour our patient grew worse and he began to be attacked by convulsions. The hiccoughing became more violent, the pains in the region of the umbilicus more intense and acute. As his strength declined, he attempted again and again to raise himself in the bed, calling upon the same death, which was now so close at hand, to succour him in his pains. At midday he began to have cold sweats, his face became corpse-like, and at sunset he died.

. . . . . .

"About fifteen hours after the death of the patient, Signor Bonioli, who was much moved at my suggestion, determined to open the body in the Scuola Medica Chirurgica of the hospital. Many physicians and surgeons were present, together with a choice band of the best instructed and most zealous of our young men. An external examination of the cadaver gave no visible signs of any alteration from the normal, neither in the matter of lividity nor in that of any great swelling of any part. The abdomen alone seemed perhaps a little swollen. The belly was opened, and scarcely had the peritoneum been torn with the knife, when there appeared a gush of semi-fluid matter, resembling in part a yellowish viscid whey. This gave out an odour like that of an acid fermentation and it amounted to more than ten pounds of our ordinary weight. This lymphatic effusion, which had poured out, covered not only the intestines, especially the small, but also in a singular manner the concave surface of the liver and of the spleen, together with all the viscera which did not lie behind the peritoneum. Not only were the superficies of these organs covered, so to speak, with the matter described above, but this same material had even formed a sort of inorganic coating or crust on the surfaces. The liver was notably greater in bulk than normal, but its substance revealed

no great change. The spleen was somewhat black, flaccid, and soft. The gall-bladder was contracted and almost empty. The small intestines seemed scarcely to have altered from their natural state. The stomach was quite empty of food-stuffs, nor did it contain more than its own particular small quantity of mucosity and in it was found no distinguishing sign of any particular disease.

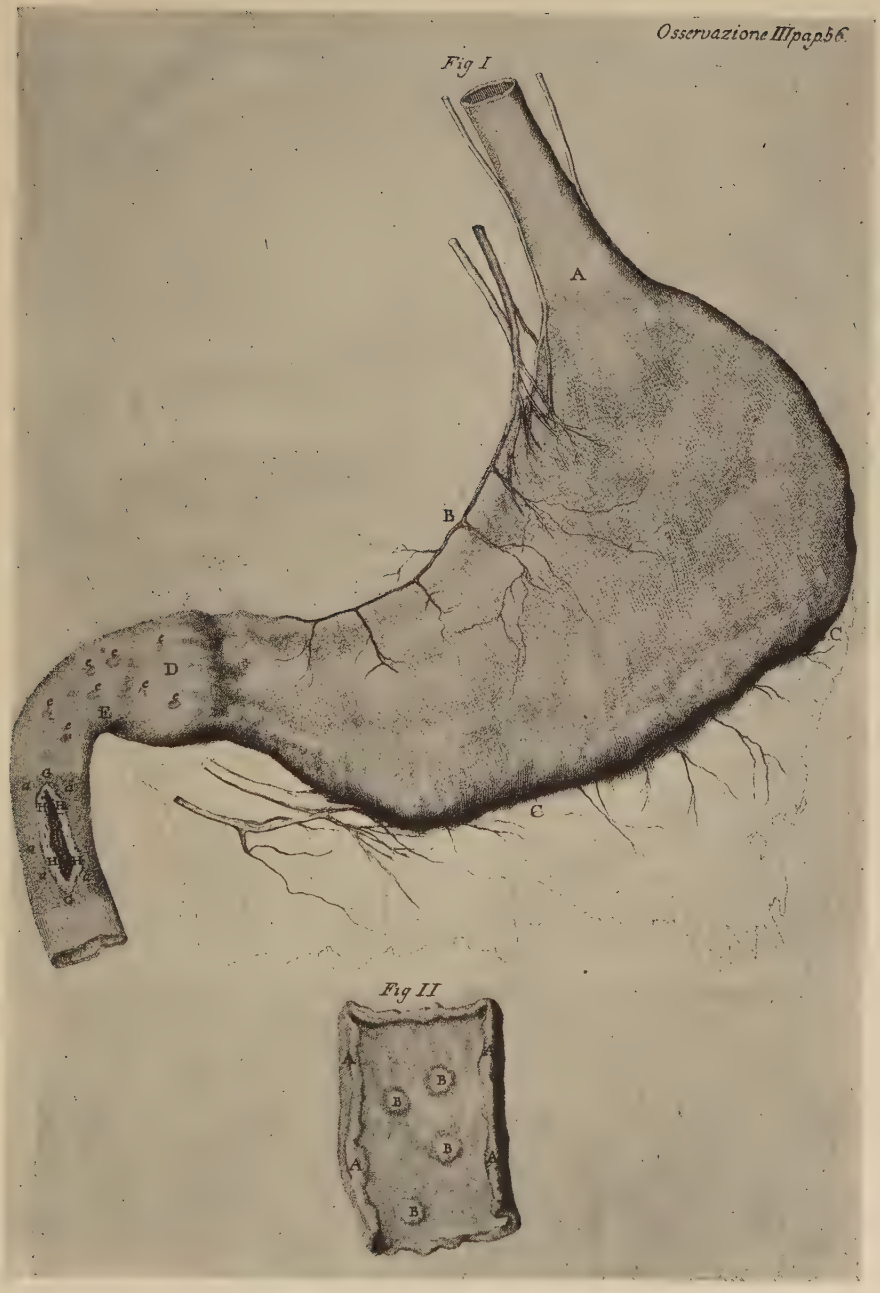
"That which formed the special interest of the present case, and is the subject of our discourse, was met with in the duodenum, as I am about to describe to you, Gentlemen. We have noticed that, suddenly when the abdomen was opened, we observed gushing forth, in a large stream, an abundance of matter very similar to the true chemical substance of the intestines and this amounted to more than ten pounds. This material not only covered the intestines, but also the viscera, and moreover it formed here, on their surfaces, a certain inorganic coating of a very strange nature. Whence this material had come could not be understood, but with more attentive observation and, after the viscera and the intestines were cleaned and wiped off with a sponge dipped in tepid water, the following was seen: Four finger-breadths below the pylorus, i.e., at the commencement of the duodenum, there presented itself to my eye a very singular oblong hole, resembling an incision made with a knife. It measured eight Parisian lines (*linee di Parig*) in length and in breadth about two. The external edge of this cleft, or one should rather describe it as a peculiar morbid ulcer, was of considerable thickness. To the touch it was sensibly hard and somewhat indurated and was turned in upon itself in a wart-like fashion; thus indicating that this peculiar local ulceration of the intestine was not of recent origin. The callous lips of this perforation were surrounded by a zone, or rather a reddened area, which reached out for about an inch around the ulcer and, shading gradually into a lighter colour, extended upwards to the pylorus and for a less considerable distance below the ulceration. Some blackish punctate markings were also noticed, scattered here and there in the reddish area. These gave some indication of the distant mortification of the parts. All the rest of the intestinal tube and the stomach itself were free from such morbid changes.

"The first figure [see plate] shows the entire organ of the stomach with that portion of the duodenum, in which is found the very strange ulcer and the perforation already described.

"The letter *A* indicates the upper portion of the stomach continuous with the œsophagus.

"*B* indicates the upper or lesser curve of the stomach.

"The two letters *C*, *C* show the greater, or rather the inferior, curve of the stomach.



PENADA'S PLATE (REDUCED).

"*D* the prominence indicating the place where the valve of the pylorus is situated in the stomach.

"*E* the place where the cavity of the stomach is narrowed after having formed the pylorus and where it becomes the duodenum.

"The two letters *G, G* give the length of the sore.

"The four letters *H, H, H, H* indicate the edges or external indurated lips of the ulcer.

"The letter *I* the centre of the perforation (in natural size) which gives entrance from the external to the internal part of the intestine.

"The small letters *a, a, a, a* show the extension of the reddened area arising from the corrosion, by which the parts adjacent to the perforation were beginning to be affected. And likewise the small letters *e, e, e, e* draw attention to the small black dots which were found, scattered here and there, in the reddened area. That portion of the intestine was opened where the sore was situated so that the state of the internal parts of the intestine could be seen. It was recognised that, in the posterior wall at the level of the ulcer, there was more than natural swelling of the coats of the intestine and these showed some projections, or small morbid lumps, scattered here and there over the internal surface of the duodenum.

"Figure 2 shows that portion of the intestine opened up, where the local morbid degeneration had occurred, and where may be better seen, in the first place, the corrosion of the internal lips of the sore and also, on the internal surface of the open intestine, that hard and unnatural substance and those prominences (or we would rather say morbid lumps) scattered here and there.

"The letters *A, A* indicate the corrosion of the internal lip of the sore. And the letters *B, B* denote those little unnatural swellings on the internal surface of the open intestine.

"Having hitherto stated the simple story of the peculiar things observed in the present case, it remains for me to complete the most interesting part of the present memoir, which, Gentlemen, is precisely this, to make plain to you, in the first place (by means of analysis and confronted with the facts which we have described) the almost absolute impossibility of localising and of identifying, merely from the appearance of the morbid phenomena, the true seat and the true internal causes of this peculiarly strange malady. I wish to point out to you, in the second place, faced by the anatomical data obtained from the investigation of the cadaver, what could have been the evidence from which one could reasonably, and with less uncertain judgment, reconstruct the series of strange phenomena occurring throughout the whole course of the illness. Finally, I wish to add whatever opinion I have formed to explain how

nature had gradually brought about that morbid degeneration of the intestines."

Penada then continues for the rest of the chapter to discuss the differential diagnosis and the symptoms of the case, the ætiology of the ulceration and the successive stages of the disease, which led to the formation of the lesions noted at the post-mortem. He had the merit of emphasising his points again and again, but this lecture must have become a little wearisome to his students!

It is clear that Penada, before the death of the patient, did not suspect ulceration. Wind in the bowel, he says, could readily explain the pain. Besides there was no fever, nor was the patient confined to his bed. Penada wonders how an accurate diagnosis could be made from these facts. Weight-lifting and heavy drinking might cause chronic inflammation of the intestines, but not ulceration. There was one circumstance in the history of the illness which Penada omitted to relate. One night Domenico Miazzo lay in a rough inn, where he had gone with a large sum of money in order to purchase sheep's carcasses and, fearing that his wealth might be stolen from him, he placed the monetary load upon his stomach and slept with an easy conscience, knowing full well that all was secure. Penada suggests that this compression of the abdomen may have started up a mild grade of inflammation, but he cannot imagine how it could cause a corroding sore of the duodenum.

Considering the findings of the post-mortem examination, Penada arrives at certain conclusions. The perforation must have occurred some considerable time before death, because the effusion into the abdomen was so extensive, because the coating formed upon the surfaces of the organs was so thick, and because the lips of the perforation were indurated. The fluid in the peritoneal cavity was the cause of the pain, but it never spread so widely as to bring about vomiting, although just before death, hiccoughing, the precursor of vomiting, began as the effect of upward pressure of the fluid upon the diaphragm. The perforation was not of a large size until a time just before death, otherwise nearly all Miazzo's food would have passed out into the peritoneal cavity and the patient's state of nutrition would have become very poor. Penada had that type of mind which sees both sides of a question simultaneously in a

strong light. In spite of what he had already said about the impossibility of the weight of money having caused the ulceration, he now suggests that this compression might have affected the tone and that gradually the coats gave way.

Penada looked over a large number of books of medicine, and although he discovered plenty of cases of ulceration in scirrhous or cancerous tumours of the stomach and records of gangrene and of sphacelus, yet nowhere did he see the record of a case like that of Domenico Miazzo.

In closing his account Jacopo Penada lays stress upon the difficulty in attempting a diagnosis of troubles in the abdomen and gives Valsalva's dictum as quoted by Morgagni—"*vigilandum, & cavendum esse in doloribus intestinorum; se enim post leves dolores, aut certe cum minime magnis; nulla manifesta febre, nullo vomitu, nulla convulsione, animo & corpore satis vigentibus, de improviso vidisse ægros in præceps ruere, & cito eripi ab lenta inflammatione, & sphacelo nec opinato intestinorum.*"

THE FUTURE OF THE CITY HOSPITALS IN LONDON

By D'Arcy Power, M.A., M.B. (Oxon), F.R.C.S. (Eng.), London

Surgeon to and Lecturer on Surgery at St. Bartholomew's Hospital; President of the Section of the History of Medicine, Royal Society of Medicine

GREECE, copying perhaps the methods of Egypt, treated the sick in Health Temples which were in direct communication with the gods. The cults of Amynos, of Amphiaraos, of Trophonius and of Asklepios are the best known, and each seems to have been conducted upon similar lines—a payment to the temple in return for which the sick man was allowed a couch in an open air ward arranged on the corridor system. He was dieted, physicked, bled, and given the opportunity of communion with the god, who either appeared in the shape of a serpent or gave directions about the cure in a vision of the night. In later years the supernatural side of the treatment became of secondary importance, whilst the store of medical knowledge amassed by the masters was taught to pupils who spread it throughout the civilised world in such a manner that it has descended to ourselves as a treasured possession in the Hippocratic writings.

Time passed; the cities became larger and their populations more numerous. The temples were replaced by institutions still on the corridor system, governed by strict rules as to cleanliness, nursing, and cookery. These institutions were under public control and the doctors in charge of them were appointed by the state. They were the immediate predecessors of hospitals as we now know them. They were not the special outcome of Christianity, for they are known to have been established at Baghdad, Cairo, and Toledo as well as in Byzantium and Cæsarea. Christianity added the dominant note of charity, which is still so characteristic of their work in this country.

Pilgrimages took many ailing persons long journeys and the hardships of travel made invalids of many who started from their

homes in the best of health. Christian charity undertook to provide for those who fell by the way and did not count the cost or grudge the labour. The merchants of Amalfi were foremost in the good work and built a hospital at Jerusalem. Thence came the Hospitallers who, even in the days of their greatest pride, still continued to enrol serving brothers to attend upon the sick poor. At first mere refuges for the friendless sick on a journey, they soon became specialised. Some, like the Hôtel Dieu at Paris or St. Bartholomew's Hospital in London, were founded designedly for the reception of those who were acutely ill, and they soon became surgical centres. Others, like St. Bartholomew's at Rochester, received patients with more chronic ailments and were thus somewhat akin to our modern infirmaries, whilst others, like the Priory of Bethlehem, charged themselves with the care of mental illness. The scourge of leprosy led to the foundation of leper houses throughout Europe, and when this disease became rare, these same lazar houses were often used to isolate patients with skin disease whether due to scabies, syphilis, or other causes.

Before the Reformation in England these hospitals were in the hands of the Church, whose members fed, treated, and attended to the spiritual needs of the inmates. After the Reformation the citizens, at any rate in London, took upon themselves the burden of charity and deputed medical men to treat the sick whilst they made themselves responsible for their feeding, nursing, and discipline. But whilst they were charitable the citizens had a shrewd eye to their own interests, for they directed their bedels that

"If in any of your walks yee shall happen to espy any person infected with any lothely griefe or disease, which shall fortune to lye in any notable place of this City, to the noyance and infection of the passers by and slander of this house, yee shall then give knowledge thereof unto the Almoners of this hospitall, that they may take such order therein as to them shall be thought meet.

"Ye shall also have a speciall eye and regard unto all such persons as have been cured and healed in this house, that none of them counterfeit any griefe or disease, neither begge within the City and liberties thereof. And if ye shall fortune to find any so doing, ye shall immediately commit him or them to some Cage and give knowledge thereof to the Governors of this house that they may take further order as they shall think best."

The system worked well for a time, but as the population increased and the town became larger many difficulties presented themselves. The sites of the older hospitals were determined by their proximity to the religious foundations to which they were originally attached and not to suitability of site or even convenience of access. They are placed, therefore, in positions which are wholly unsuitable from the health point of view, often in the heart of the city, surrounded by noisy streets and overlooked by high buildings. Under such conditions land is too valuable to allow of necessary expansion, and the greatest economy of space barely allows for efficient working. The nadir of hospitals was reached in all probability about the middle of the last century, when the advance of surgery enabled a larger number of important operations to be performed than had ever been undertaken previously. At this time the science of public health was in its infancy and bacteriology was as yet unborn. The part played by microbes in causing disease was not recognised, and no precautions were taken to limit their action. They held undisputed sway and thence came the appalling tragedy of men and women dying of diseases contracted in the very institutions set aside for their cure. Mid-wives and surgeons learnt the lesson first, for the ravages of infecting microbes were ever hampering their efforts. Semmelweis nearly attained to the truth by empirical means, but the full glory of achievement was left to Lister, who gained his knowledge by the sound method of experiment.

Bacteriology being thus started on its beneficent career and the life history of the pathogenic organisms being known, it has not been difficult to fight them until the mortality from sepsis has become negligible in the wards of a well-conducted hospital. Public opinion, however, has lagged behind the pioneers, and the corporate conscience has not yet been sufficiently awakened to allow of the same drastic methods of dealing with infective disease outside the hospitals as are proved to be effectual in the surgical and lying-in wards of every public institution. Something, however, has been done, for smallpox and typhus have almost disappeared, whilst the autumnal epidemic of typhoid fever which used to be so fatal has now been greatly reduced.

Epidemics of measles, scarlet fever, chicken-pox and whooping

cough are much too frequent, and the common belief still remains that these and other "childish" diseases are inevitable. The recent findings of the recruiting Boards in England show how much has yet to be done in the prevention of preventable disease and how serious are the sequelæ of many of them in connection with the general health of the population. Colonel J. G. Adami has recently published the following table of the causes of rejection, owing to infections and their results, in 1814 cases in a single industrial (mining) centre:

Disease	No. of Cases	Percentage of Rejections	Percentage of Total Examined
Tuberculosis *	584	31·6	2·3
Valvular disease of the heart	188	9·0	0·7
Infantile paralysis	69	3·7	0·29
Otorrhœa	41	2·2	0·17
Chronic bronchitis	39	2·1	0·15
Rheumatoid arthritis	26	1·4	0·1
Disordered action of the heart	10	0·5	—
Totals	957	50·5	—

* Pulmonary tuberculosis, 468 cases or 25·3%

The table is full of instruction and has a direct bearing upon the future of the City Hospitals in London. It shows that 50 per cent of the physical disability is caused by microbic infection and should therefore be preventable. If they were prevented half the beds in a hospital would be sufficient, but it is probable that the patients who filled these beds would be more acutely ill than they are at present.

The majority of the hospitals in the City of London remain on the site where they were originally built, partly because they have always been there, partly because it was thought that the convenience of the patients and of the medical staff was best consulted by leaving them where it had suited the convenience of former generations. Our forefathers were content to drive or even to walk, and times and distances are still measured in terms of these forms of locomotion. The whole system of traffic was changed with the invention of the internal-combustion engine, and we think no more of ten miles in a motor car than our ancestors did of travelling two. It should be quite possible, therefore, to change the present system of having a central hospital in the heart of the city and a con-

valescent home ten miles away for a parent hospital in the country and a nucleus in the city. London is very favourably placed for such an arrangement. The town in its busiest parts lies only a few feet above sea level, but it is surrounded by higher ground which is especially rich in commons and open spaces. Many of these open spaces have been secured for the use of the public and can never be built upon, but they nearly all have a fringe or even oases of buildings of which it is still possible to obtain possession. Such sites are of sufficient size to allow of the erection of buildings suitable for a large hospital. It would be easy to build a hospital on parts of Wimbledon Common, Banstead Downs, Hampstead Heath, the lower part of Epping Forest or the immediate neighbourhood of Chipping Barnet, all places which can be reached by motor car within half an hour from the centre of London. In any of these places it would be possible to return to the Greek ideal of a hospital —the provision of plenty of air and sunlight—for the experience of the recent war has shown that even in London there are many months in the year when bedridden patients can be kept out of doors for the whole day if some slight protection is afforded. Something has already been done in this direction by the erection of verandahs and open-air shelters in the City Hospitals, but the grime of a large town almost outweighs the advantages gained. With more space and cleaner surroundings the patients would make a more speedy convalescence and much could be done to while away the weary hours whilst they were making progress to recovery.

If the main hospital were transferred to a site outside the city it would still be necessary to maintain a nucleus where the most acute cases could be operated upon and where out-patients and walking cases could be seen. A few beds would be needed for the treatment of such emergencies as acute intestinal perforation and obstruction, machinery accidents, and the severe injuries incidental to the traffic of a large town. The beds, however, need not be numerous, because provision should be made to remove the patients to the main hospital in the course of a very few days. The out-patient department would necessarily be upon a larger scale, since accommodation would have to be found for the patients attending the ophthalmic, aural, laryngological, obstetric, and venereal clinics.

The staffing of the hospital under such altered conditions would

not involve any great change. It could easily be arranged that the younger generation who now occupy the posts of assistant physicians and assistant surgeons should attend at the City nucleus, where in addition to the acute emergency cases they would treat the out-patients as they do at present, whilst the senior medical officers would attend the main hospital, which should be under the control of a resident medical officer with a sufficient number of qualified assistants.

The hospitals are important centres of medical education, and accommodation must be provided, therefore, for the students and for their education. Before entering the hospital these students should have finished the anatomical and physiological parts of their studies at a central institution, and it should only be necessary to provide for their clinical and pathological teaching. It would, moreover, be to the advantage of the students both for discipline, health, and instruction that they should live in the immediate neighbourhood of the hospital and in a college such as already exists in connection with many of the larger hospitals.

The clinical teaching in the wards would be undertaken by the senior members of the staff, since it is very desirable that the foundations of knowledge should be well and truly laid, and this is best done by those who have had the greatest experience. At the end of a year spent in the wards and laboratories of the main hospital the students should attend the City nucleus to see the emergency work and to obtain from the junior teachers the latest additions to medical and surgical knowledge. A good finish would thus be given to a thoroughly sound education. At the present time, too, every first-rate hospital is a training school for professional nursing. Provision for teaching nurses, therefore, must also be provided if nursing as a profession is to be maintained at its present high level or is still further to be improved upon.

The nurse's training is hampered by the fact that she is worked too hard, is given too little time for study, and is without any time at all for recreation and general education. The fault appears to lie in the understaffing of hospitals, or rather, in working with too small a reserve to allow for sickness and necessary holidays. The situation of a hospital in the centre of the city does not allow a nurse to get sufficient air and exercise during her short periods off duty. A stroll

in the neighbouring streets, a ride on an omnibus or in a tram is her usual relaxation. There is no pleasant place where she can sit and rest, no place where she can play tennis or hockey even if she felt inclined for such exertion. The wonder is that so many nurses retain their health and strength in spite of the long hours spent in the exacting duties of the wards and operating theatres.

The nurse, then, has much to gain by the removal of the main hospital into the country. Her work could then be carried out in the fresh air; there would be space for a recreation ground; sleep would be sounder and more refreshing away from the noises of the City and she would thus be the better fitted to take her tour of duty at the City nucleus when it was required of her.

The financial aspect of such a change would have to be carefully scrutinised before it was embarked upon, but it would not at first sight appear to present any insurmountable difficulties. The older hospitals now occupy considerable spaces in the very heart of the City, where land sells by the foot at exorbitant prices. The land to which the hospital would be removed is of much less value, and it is probable that the difference in the selling and buying prices would more than pay for the new buildings and the cost of transfer. It would not, therefore, be necessary to invoke the assistance of the State, nor would it be desirable to eliminate the element of charity which has always been so marked a feature in the conduct of hospitals in England.

THOMAS TROTTER, M.D.

By Sir Humphry Rolleston, K.C.B., M. D. (Camb.), F.R.C.P. (Lond.)

Emeritus Physician St. George's Hospital, London; President of the Royal Society of Medicine

THE peculiar interest in the lives of those who have striven and deserved but have not attained success as ordinarily estimated may be prompted by various reasons; partly by speculation as to the causes of this failure and partly by sympathy with the want of the arts of success and with betrayal by the fickle Goddess, for according to Samuel Butler in "Hudibras"

> Success, the mark no mortal wit,
> Or surest hand, can always hit.

The man who fails to achieve the reputation or recognition which he considers his due may according to his disposition be thus either embittered or stimulated by divine discontent to outdo his former efforts. There is indeed something to be said in favour of triumph deferred and specially of not attaining the supreme ambition, for when this is done the restless energy that inspired activity may be met by the question what farther object is there for life and labour. Examples of collapse and death soon after, and possibly favoured by, the advent of the prize long awaited would not be difficult to quote. The manner in which success or failure is borne is an index of character, and though it may be true that success is more difficult to bear than the reverse, the problems involved by apparent failure are the more interesting. But here we can hardly avoid the question, What is true success? Shall we agree with Macbeth that it is the possession of "honour, love, obedience, troops of friends," or that it turns on the verdict of posterity such as may be very roughly estimated by inclusion in the Dictionary of National Biography, which may indeed be merely evidence of notoriety, or that it is something higher though less tangible and suggested in a negative fashion by the reflection "What shall it

profit a man if he gain the whole world and lose his own soul?" The narrower question of what constitutes success in the medical profession would serve, and possibly has been used, as an attractive text for the old-fashioned introductory address at the beginning of the winter session. But meanwhile two *obiter dicta* on the subject may be quoted. Cabot in his recent "Training and Rewards of the Physician" (1918), points out that to the world apparent failure may mean more than success, and that many an inventor has failed to earn a living. Thomas Young, the most comprehensive genius and greatest man of science who ever became a member of our profession, was not a success in practice, being regarded by the students of St. George's Hospital as "a great philosopher but a bad physician." In discussing the relation between ability and success he makes the rather remarkable statement that "However inadequate the possession of superior talents alone may be to ensure the confidence of the public, it must be a mistaken opinion, although it has been asserted by persons of no ordinary observation, that a man of great abilities is morally incapable of being a good physician." (1)

These remarks are by way of introducing and perhaps justifying the choice of Thomas Trotter, Physician to the Fleet, a would-be reformer of the Medical Department of the Navy, and poetaster, as the subject of this short contribution. Though included in the Dictionary of National Biography he is practically forgotten, and it is only too obvious from his writings that he was not satisfied with his lot; thus more than once he rather querulously complains of the opposition and hostility offered to his measures of reform in the Navy. He was overshadowed by his senior contemporary Sir Gilbert Blane, whom in company with the elder Lind he not infrequently criticised and more rarely praised. Blane attained a lasting position of authority in the Naval Medical world after less than four years' (1779–1783) service afloat, thereby gaining a pension of ten shillings a day, subsequently raised in 1802, on the conclusion of his work on the Board of the Sick and Hurt, to a pound a day, and spent the rest of his life in London engaged in a lucrative practice and moving in the highest medical circles of the day. Though Trotter often refers directly or indirectly to Blane, he does not appear to have obtained any public recognition in return; and more-

over when he retired in 1802 his pension (£200) was much less than that awarded to his elder Scottish colleague, although they began their sea service about the same time—Blane in the first instance (1779) as private physician to Sir George Rodney, who very shortly afterwards appointed him official Physician to the Fleet, and Trotter in 1778 as Surgeon's Mate, a progress prophetic of their future positions. It is perhaps only extremely human of Trotter that he did not love his more successful colleague.

Thus Trotter attacked Blane indirectly in his letter to Lord St. Vincent containing among his "proposals for meliorating the establishment of medical officers" the recommendation that no surgeon should be promoted to the rank of physician under five years' service, and that their degrees should be obtained in a regular manner from the universities where they have studied the usual number of terms. (2) In his list of three physicians who have fulfilled the last condition his own name appears, but not that of Blane, and he adds a note that all the others including all the Commissioners of Sick and Hurt (Blane was a member at this date, 1801) have obtained their M.D. degrees by proxy elsewhere. Blane, it may be noted, was made Physician to the Fleet after a few months' service and took his M.D. degree at Glasgow after being educated at Edinburgh. Trotter also inveighed against Naval Medical Officers engaging in private practice, then allowed but forbidden the next year, and evidently has an eye on Blane in his dictum that "nothing can be more indecent than a member of a public board traversing the Metropolis in the private practice of his profession . . . it appears to me that the man who decoys a Commissioner of the Sick and Hurt, a Physician of the Fleet or Naval Hospital, to give advice for a guinea is guilty of something that approaches near bribery and liable to prosecution." These pronouncements were hardly likely to curry favour with the powers of the Commissioners of the Sick and Hurt, and to do him justice Trotter seldom adopted an obsequious course, though on one occasion he confessed to having "endeavoured to imitate Dr. Blane in calling upon the Surgeons for occasional remarks" for publication in his "Medicina Nautica," and elsewhere observes that Dr. Blane has "very successfully directed his eminent talents" to preserving the health of seamen.

A few words may be added about Trotter's attitude toward Lind (1716–1794), who was very much his senior and had retired from Haslar in 1783, some eleven years before Trotter was appointed there, for it is marked by alternations of praise and rather acid criticism. He speaks of him as "the Father of Nautical Medicine," (3) and elsewhere writes "of great medical abilities that have attended Military services, the Army of the country can boast of a Pringle, a Cleghorn, and a Monro and some others who have written since the last war, but the name of Lind stands alone in the Navy." (4) Possibly this panegyric also served as a cut at Blane, who had by this time (1792) brought out the second edition of his well-known "Observations on the Diseases of Seamen." On the other hand, Trotter rather unfairly depreciated Lind's treatment of scurvy with lemon juice, and expressed his surprise that Lind had had so many opportunities of examining cases of scurvy after death, and adds, "the plain truth of the matter is, his method of cure was imperfect, for a man dying of scurvy is not known at the present day," yet in a previous sentence he refers to sailors dying from scurvy while being conveyed to Haslar where Lind was in charge. It is certainly very unfair to saddle Lind with the results of failure to carry out the treatment advocated by him. Again while referring to W. Cockburn's writings on scurvy (1706) and the dependence of the disease on the indigestible character of the diet he adds, "from which it is easy to see where Lind took his opinions of the production of the disease." As reference to Cockburn's work shows that scurvy was attributed to salt, this hardly appears justified. Lind's method of disinfecting wards by fumigation was another favourite butt of Trotter's, who preferred fresh air and ventilation and insisted on the value of a hyper-oxygenated atmosphere in enabling the body to resist infection. Lind, it is only right to point out, while emphatic as to the value of fresh air and cleanliness in preventing the spread of infection, fully recognised that these means alone might not be sufficient to destroy the infection, and for this purpose employed fumigation by tobacco burnt with junk, or by charcoal fires strewn with sulphur or arsenic.

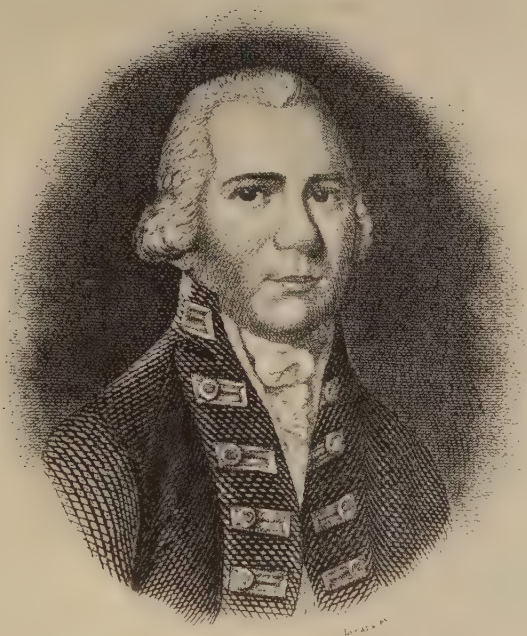
This brief survey of Trotter's relations to Blane and Lind certainly shows him in a rather unattractive light, but it should be remembered that his position must have been very galling and that

the medical spirit of the times was nothing if not outspoken, as is strikingly shown by the fictitious "intercepted letters" written by James Wardrop in the *Lancet*. At any rate it illustrates Trotter's character and his methods as a critic and fighter.

Thomas Trotter was born at Melrose in Roxburghshire in 1760 according to the Dictionary of National Biography, or in 1761 as stated by Cockburn (*5*) in much the longest and most eulogistic account of him that I have seen. He was the eldest son of John Trotter, another of whose sons, Andrew, also entered the medical profession and practised at North Shields. After attending a school at Kelso Thomas studied medicine at Edinburgh and while there published some short poems in the *Edinburgh Magazine* (1777–8). In 1779 he became Surgeon's Mate in the *Berwick* in the Channel and began his practical acquaintance with scurvy. In 1780 the *Berwick* sailed for the West Indies and in October was much damaged in a hurricane, the medicines and medical comforts being lost. As a result dysentery and scurvy took a heavy toll of the crew on the voyage back to England, and Trotter suffered severely. After refitting the *Berwick* went to the North Sea and took part in the Battle of the Dogger Bank on August 5, 1781, Trotter receiving the public thanks of Commodore Stewart for his services to the wounded. In April, 1782, he was promoted surgeon, but in the following year only 120 of the 750 surgeons in the navy list were allowed on a small half pay, and as peace had led to a great reduction in the number of posts he was left unemployed. He accordingly went in June as surgeon in the *Brooks*, a Liverpool guineaman or slaver, to the Gold Coast, where eleven months were spent in collecting slaves; scurvy began to appear before they sailed and, as Trotter's recommendations to lay in a good stock of fresh vegetables were disregarded, became rampant on the voyage to the West Indies, forty slaves being buried before reaching Antigua, where an abundant supply of fresh fruit was obtained; a fortnight later on their arrival at Jamaica the slaves, now free from scurvy, were sold for high prices. Here Trotter was severely attacked with fever from which he had barely recovered when he arrived in England in September, 1784, so disgusted with the horrors of the slave trade that nothing would induce him to undertake another voyage. Soon afterwards he returned to Edinburgh for further medical

work and published his "Observations on Scurvy" (1786). After practising for a time at Wooler in Northumberland he read his thesis for the M.D. Edinburgh, "De Ebrietata" (1788), a subject which *mirabile dictu* had never previously inspired a thesis at this seat of high thinking. In 1789 he was appointed to the *Barfleur*, the flagship of Admiral Roddam at Portsmouth, and had further opportunities of investigating scurvy, thus providing material for the second edition of his brochure on the subject (1792). At this time he investigated the preservation of drinking water in casks with a view of preventing the objectionable taste that the water commonly acquired. This he ascribed to the oxygen of the water being attracted to the wood with the liberation of free hydrogen, and to obviate this he recommended that the inside of the barrels should be burnt or charred. About Christmas, 1793, he was appointed second physician to Haslar, an office which he took up with great energy, making many changes in the organisation as may be seen in his pamphlet, "Remarks on the Establishment of the Naval Hospitals with Hints for their Improvement" (1795), dealing with the Staff and their payment, nursing, baths, diet, and the grounds. Rather optimistically he considered that in the future the baths of Haslar should be as famous as those of Baiæ in the days of ancient Rome. He, however, did not remain long at Haslar, for on April 9, 1794, he became Physician to the Channel Fleet under Lord Howe, this unsolicited appointment being regarded by him as due to his work on scurvy. His term of office was one of great naval activity and he was correspondingly energetic, not only in his routine duties but also in writing; his "Medical and Chemical Essays" appearing in 1795, Volume II of the "Medicina Nautica" seeing the light in 1799, and "Suspiria Oceani; a Monody on the Death of Lord Howe, K.G., Admiral of the Fleet" (23 pages) in 1800. His work must have been carried out under difficulties, for in June, 1795, while going up the ship's side to the relief of a wounded officer he sustained a rupture which before his retirement in 1802 incapacitated him from boat work.

After his retirement from the Navy he practised as a physician in Newcastle until 1827, when from increasing disabilities he gave up active medical work; after spending some time in Roxburghshire and Edinburgh he returned to Newcastle and died on Septem-



Dr TROTTER

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ber 5, 1832, two years before Blane. During the years succeeding his retirement from the Navy his pen was constantly at work on such various subjects as "A View of the Nervous Temperament" (1807, 3d Edition, 1812, pages 378), "A Proposal for Destroying the Fire and Choak-damp of Coal-mines" (1805), "The Noble Foundling, or the Hermit of the Tweed, a Tragedy in Five Acts" (1812), "A Practical Plan for Manning the Navy and Preserving our Maritime Supremacy without Impressment" (1819), and "Seaweeds, Poems Written on Various Occasions Chiefly During a Naval Life" (1829), with a rather long autobiographical introduction and a line engraving by Lizars representing the author at the age of 37. This (Fig. 1) was presumed by Laughton to be after a portrait by D. Orme, but it differs considerably from a stippled engraving (Fig. 2) by Orme, of which there are three copies in the Royal Society of Medicine, two in the collection of the Royal College of Physicians, and one in the British Museum, published on May 1, 1796, when Trotter was in his thirty-sixth or thirty-seventh year. For this copy I am indebted to my friend Arnold Chaplin, Harveian Librarian at the Royal College of Physicians. The representation in "Seaweeds" is the more attractive of the two, and, as it apparently shows the author in a uniform which was not given to medical officers of the Navy until 1805, (6) it seems not unlikely that it was, if based on Orme's portrait of 1796, modified at the sitter's direction in various ways before it met the public eye in "Seaweeds." But although some time has been spent in attempting to clear up the minor questions raised by these two portraits no definite conclusion is perhaps justified.

As already shown, Trotter was a prolific writer in a wide field of subjects; but although several of his works, "Medicina Nautica," "A View of the Nervous Temperament," "Observations on Scurvy," and his graduation thesis "On Drunkenness," passed into a second edition, they are not easy to obtain. Out of the thirteen books and pamphlets mentioned in Laughton's biography in the Dictionary of National Biography, which omits the "Remarks on Naval Hospitals and Sick Quarters with Hints for their Improvement" (1795), there are eight in the British Museum, while the London Library, The Admiralty Library and the Medical Libraries in London contain as a rule one each, the library at Haslar has two and the

Royal College of Physicians of Edinburgh four of his fourteen publications. After the lapse of 100 years or more many of his views, especially those on chemistry, necessarily appear crude. On the other hand, looking at Trotter across a century containing the era of morbid anatomy which had hardly dawned in his early days and now unfortunately is passing too much into the shade, as has been hinted in the late Sir James Goodhart's Harveian Oration on the passing of morbid anatomy (1912) and recently more decidedly expressed by Christian (7) of Boston, it appears that the pendulum is swinging back to the point of view of Trotter's time, and that chemical and functional problems are taking the place of structural questions. The present discussions in acidosis and the buffer salts have their prototypes in the speculations of the "pneumatic" and other physicians. It is, therefore, interesting to refer here to Trotter's views on scurvy, one of his favourite subjects. He believed that the disease was due to a deficiency in the blood of oxygen, which was regarded as the "acidifying principle," and that this could be made good by the administration of citric acid. While stating that for the prevention of the disease fresh vegetables should be relied on, his experience led him to distrust the use of preserved lemon juice as a prophylactic and he ascribed this failure to its frequent adulteration with acetic acid. For curative purposes he strongly urged concentrated, or as he called it concrete, crystallised citric acid in solution. The Commissioners of the Sick and Hurt Board, among whom was Blane, did not support Trotter's advocacy of pure citric acid. This difference of opinion is curiously paralleled by quite recent events, since Funk's description of vitamines in 1910 scurvy has been regarded as a "deficiency disease" and due to the absence of an antiscorbutic substance contained in lemon and orange juice. But McCollum and Pitz (8) have shown that artificially induced scurvy in guinea pigs can be cured by an imitation orange juice consisting of pure inorganic salts, cane sugar, and crystalline citric acid, thus agreeing with Trotter's ancient contention, and they further conclude that scurvy is not an avitaminosis, but due to bacterial infection resulting from fæcal accumulation caused by unsuitable food. On the other hand, Harden and Zilva (9), after removing the free citric and other acids from lemon juice, found that the residue cured scurvy in infants under Still's care, and so obviously retained its antiscorbutic activity.

Of his numerous works much the largest is "Medicina Nautica," in three volumes with over 1400 pages in all, which came out in 1791, 1799, and 1803, and passed into a second edition in 1804; in 1798 the first volume was translated by Warner into German, with a preface by Hufeland, who, while faintly commending it, reserves most of his praise for the translator on account of the unusual difficulties he had to encounter in the author's style, which is said to be often obscure and abounding with "many almost incomprehensible nautico-technical expressions." It is a collection of articles on naval medicine, parts of which recall the works of Lind and Blane. Thus it contains the medical history of the Fleet from January, 1794, to the termination of the war in April, 1802, and so resembles Blane's "Observations on the Diseases of Seamen," based on a detailed account of the health and diseases of the Fleet from 1780 to 1783. Trotter also describes various diseases, especially fevers and scurvy, in a text-book manner, thus again resembling Lind's and Blane's books. In addition he introduces into the second and third volumes cases by naval surgeons, so that to some extent these volumes resemble the proceedings of a medical society in which the president does most of the talking. Incidentally it contains items of autobiography, such as a list of the sixty-eight subscribers to a massy urn with a Latin inscription presented to him by naval surgeons on his retirement in 1802. These volumes perhaps naturally repeat a good deal of what he had previously written in scattered publications. The two following clinical cases may perhaps be quoted:

In "a case of supposed phthisis from swallowing a plum-stone," (10) vigorous treatment with digitalis caused violent vomiting and the expulsion of a plum-stone, which had presumably induced purulent bronchiectasis; and from this time the patient previously regarded as certain to die steadily recovered. Digitalis was thought to have rendered the most prominent features of the disease stationary, but in the light of the present day it did good by its emetic effects which led to the removal of the plum-stone.

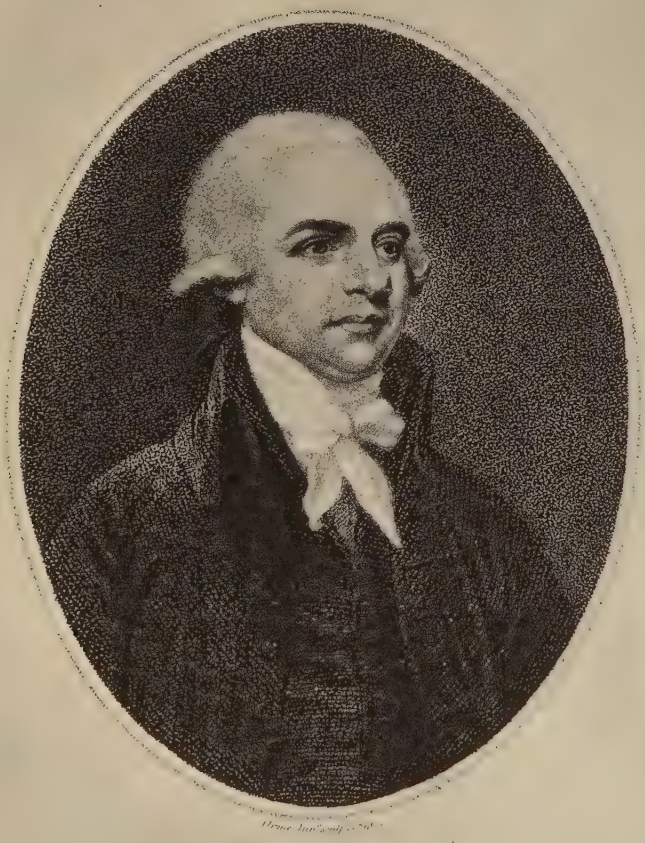
In the "Medical and Chemical Essays" (1795) he describes the case of a blue boy who died in Haslar apparently with ante-mortem clot in the right auricle, "two vesicles like hydatids near the opening of the pulmonary artery, each about the size of a large oval bean," pulmonary

apoplexy, right pleural effusion, and œdema, and adds, "I shall make no comment on this singular case, but leave the pneumatic physician to account whether this obstruction in the auricle was the cause of the blood not being fully oxygenated by the blood."

His considerable work entitled "A View of the Nervous Temperament, being a Practical Enquiry into the Increasing Prevalence, Prevention and Treatment of those Diseases Commonly Called Nervous, Bilious, Stomach and Liver Complaints, Low Spirits and Gout," provides solid reading. He finds that the eighteenth century was remarkable for the increase of nervous diseases and that whereas in the "English Malady" (1733) George Cheyne of Bath and London estimated that one-third of the upper classes were thus affected, Trotter says that nervous diseases constitute two-thirds of all the disorders of civilised society, attack the poor as well as the well-to-do, and are tending rapidly to abridge the physical strength and mental capacities of the human race. The remedy is a return to the simple life.

The appearance in 1805 of his pamphlet of 47 pages, "A Proposal for destroying the Fire and Choak-damp in Coal-mines," by fumigation and water at 40° F. run in by a fire-engine, was followed by a wordy warfare; in 1806 "A Friend to Rational Improvement" attacked Trotter in a brochure of 46 pages, and almost at the same time H. Dewar, M.D., Honorary Physician to the Manchester Infirmary (1804–6), poured out 53 pages of chemical and other strictures on Trotter's proposals. To these Trotter at once replied, but the "Friend to Rational Improvement" had the last word in August, 1806. These five polemic exercises are bound up in one volume in the Library of the Royal Medical Society of Edinburgh; but they have long been buried in oblivion, as in 1815 Sir Humphry Davy brought out his safety lamp for miners, which also raised a small storm for priority with George Stephenson, the future pioneer of railway enterprise, and in its turn has been superseded by the electric light.

"The Practicable Plan for Manning the Royal Navy and Preserving our Maritime Supremacy without Impressment" (1819) is not without interest in connexion with recent events, for it gives an account of the general mutiny in the Royal Navy in 1797 for increase of pay and rations, of which Trotter as serving under



Drawn from the Life by Artist

Thos. Trotter M.D.

(PHYSICIAN to the GRAND FLEET.)

Published as the Act directs May 1st, 1806.

Admiral Lord Howe must have had first-hand experience. He uses the mutiny as an obvious argument against the press-gang system, which naturally led to discontent and favoured the occurrence of such disturbances, and advocates a voluntary system based on Pitt's emergency Bill of Requisition in 1795. This paper also reiterates the suggestion of a uniform for sailors which, however, did not become established until about 1857; before that date the captain of each ship determined the style of clothes or "slops"—often somewhat piratical—of the crew. As far back as 1774 Lind (11) had suggested that the seamen of His Majesty's service should be put into a uniform sea habit with some little movable badges to show their ship, and urged this with a view of preventing the spread of infection by filthy clothing. This was supported by Blane and elaborated by Trotter, (12) who proposed that the uniform, manufactured of a particular form of cloth, should consist of a blue jacket, with a sleeve and cape of the same, and lined with thin white flannel; a waistcoat of white cloth, trimmed with blue tape; blue trousers, or pantaloons, of the same cloth as the jacket, for winter; and linen or cotton trousers, either striped blue and white or all white for summer. A button of metal, or horn less liable to tarnish, with the letters R. N. upon it. The hat small and round, waterproof, with a narrow belt on which should be printed the name of the ship, which could be conveniently shifted when a man turned over to another ship. It would appear that after the decent interval of sixty years Trotter's suggestions were largely adopted. He argued that in addition to the sanitary advantages the adoption of this uniform would be considered an honourable distinction, engender *esprit de corps*, and render desertion less easy.

After what has been said it is hardly necessary to insist at length on Trotter's long-continued interest in the welfare of the men, and especially of the Medical Department, of the Navy, dating from his pamphlet, "A Review of the Medical Department in the British Navy, with a Method of Reform Proposed," published in 1790, when he was about thirty years old. At Haslar he did much in improving the care of the patients and urged the institution of medical libraries and medical schools there and at Plymouth. The want of proper discipline at these hospitals which were staffed by rather turbulent officials, both male and female, and full of law-

less sailors anxious to escape from what they regarded as a prison, was a serious question and, although the reform was not always free from friction, Trotter appears to have been fully justified in reporting on December 26, 1794, that the presence of an executive officer was necessary to keep the seamen in order. The appointment of Captains, R. N., as Governors of the Naval Hospitals at Haslar and Plymouth occurred in 1795, the title being changed in 1820 to Captain-Superintendent, and continued until 1869, when the sole control was vested in a medical authority—an Inspector-General of Hospitals and Fleets. While in charge of the Fleet Trotter did his utmost to improve the sanitary and dietetic conditions of the men, stimulated the medical officers to an interest in their professional duties and insisted in demanding an increase in their pay so that they should be on an equality with the medical officers of the Army. That these efforts were appreciated by the medical officers seems clear, for on two occasions at least they shewed their esteem in a practical form: in 1797 fifteen surgeons of His Majesty's Ships at the Cape of Good Hope sent him a gold snuff box "in gratitude for long and unwearied exertion on behalf of the surgeons" and, as already mentioned, he was the recipient of a massy urn on his retirement in 1802. Jennerian vaccination at once found in him a warm advocate, but his attempt to introduce it into the Fleet was not encouraged by the higher authorities; he suggested that "as titles and pensions have rapidly crowned the heroes of the war, the Minister of Peace (the accomplished Mr. Addington, the son of a physician) should hasten to reward the benefactor of mankind with a suitable dignity." Acting up to his own doctrine he inspired 89 naval surgeons to present Edward Jenner with a gold medal in 1801. In 1819 Blane urged the importance of vaccination in the Navy, but it did not become compulsory till about 1858. In another direction Trotter successfully faced unpopularity and, as he records, the prophecy that he would be found murdered in the streets, by getting the licensed gin-shops in Plymouth reduced from 300 to 100. After 1795 as a result of the adoption of the precautions urged by Lind more than forty years before, scurvy disappeared from the Navy, but it still occurred in the ships of the East India Company, and Trotter had the foresight to urge that a commercial country such as Britain should

have a Board of Health to supervise the well-being of the Mercantile Marine, especially on long voyages during which scurvy was prone to occur. In conclusion, whatever his faults of taste, Trotter was a reformer and deserved well of the Navy for his tenacity and energy.

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ON A MINIATURE, ASCRIBED TO MANTEGNA, OF AN OPERATION BY COSMAS AND DAMIAN

By Charles and Dorothea Singer, Oxford

Μέμνησο ἀπιστεῖν

THE legends of Cosmas and Damian took their rise in the East during the early centuries of the Christian era. Some see in the Greek accounts that rose around the names of these two saints a reflection of the cult of the Dioscuri, while anyone who reads the life of Apollonius of Tyana will be struck by the fact that in the fourth century there was a collection of stories which bear many resemblances to those of our two saints. However the legends of Cosmas and Damian took their origin, they were certainly widespread in the Eastern Empire in the early Middle Ages, and we have several Greek MSS. of the ninth or tenth centuries containing accounts of the twin wonder workers. With the eastern development of the legend we are not now concerned, but the subject has been very thoroughly investigated in a series of able works of which we append a bibliography.

A cult of the saints reached the West at least as early as the sixth century and was well known in the Middle Ages. The legend became finally elaborated into the form that we here roughly sketch, our version being an abstract of that given in the "Actes des Martyrs," published by the Benedictines of the Congregation of France.

Cosmas and Damian were twin brothers of Arabian origin. They were born of Christian parents and their activities were carried on mainly at Ægæ on the Gulf of Issus in Cilicia, where they are said to have lived in the second half of the third century. The brothers early applied themselves to learning and especially to the art of medicine, and they rapidly acquired such fame that crowds flocked to be healed by them. Their cures were performed not only by the exercise of their art, but frequently by divine assistance, which was granted them on account of their pious lives and devotion

to the poor, for they always refused payment and were therefore called *Anargyri* (feeless). On a certain occasion Damian fell so far as to accept three eggs as a reward for his treatment, and this led to an estrangement between the brothers, healed only by divine intervention.

After the brothers had been performing their cures for some years it came about that some ill-disposed fellow went to Lysias, the Roman governor of Ægæ, telling him that there were two Christians parading the neighbouring country healing the sick, exorcising unclean spirits, working miracles, forbidding the sacrifices to the gods in the temples, and doing all these things in the name of Christ. Haled before Lysias, they admitted the truth of the charges. The governor then commanded them to offer incense to idols, but they refused, saying, "Do what thou wilt, we fear not thy tortures, for Christ is our aid."

The story tells that they were then submitted to a series of tortures, but emerged victorious from them all. First they were scourged, but they prayed the while and the thongs did them no harm and they besought trials yet more hard. Then they were hung about with chains and plunged into the sea, but an angel broke their bonds and drew them to the shore. Brought again to the court, Lysias confronted them with the question, "Will ye now make sacrifice or persist ye yet in your madness?" The martyrs made answer, "We are Christians, nor will we at all forswear our Lord nor sacrifice to unclean idols and senseless stones." They were then hurled upon a burning pyre, but not a hair was singed. This failing, they were stretched upon the rack and flogged, but still no sign of pain escaped them. At last Lysias exclaimed, "The gods shall witness that I be not conquered by your witchcraft, for I will give you yet further anguish and then fling your carcases to birds of prey." To which the saints replied, "Since we have in heaven a King eternal, our Lord Jesus Christ, we fear not thy torments."

Lysias then had them suspended upon crosses and while they thus hung they were stoned and shot at by his archers. But stones and arrows alike fell back from them harmless, until at last the exasperated governor struck off their heads with a sword. In dying the martyrs chanted, "It is a good thing to give thanks unto the Lord and to sing praises unto Thy Name, O Most High."

The bodies of the two brothers are said to have been buried at the neighbouring Syrian town of Cyrrhus, where Theodoret (386–451), who was bishop of the See early in the fifth century, speaks of a church dedicated to Saints Cosmas and Damian, "the illustrious warriors, the holy athletes of Jesus Christ," and in the following century Justinian honoured the town for the sake of the remains of the saints, by whose intervention he had been healed of a mortal disease.

The cult of Cosmas and Damian appeared early in Italy, and it is said that a church was dedicated to them at Rome by Pope Felix IV. in the sixth century. The church of Cosmas and Damian still existing in the Forum is said to be on the ancient site of this building and it possesses a mosaic of very great antiquity containing effigies of the two saints. Rome possesses two other churches dedicated to Cosmas and Damian. One is in the Via dei Barbieri, and with it the Corporation of Barbers has become associated. Among the other Italian churches dedicated to Cosmas and Damian is that near Subiaco in the monastery of Santa Scholastica, interesting as the site of the earliest printing press in Italy (*first works* Donatus, Cicero, and Lactantius, 1465), and still possessing a superb collection of incunabula.

The 27th of September has been set apart by the Roman Church in honour of the twin physicians, and they are commemorated in a passage in the Canon of the Mass together with a number of local Roman saints. Since the Canon of the Mass is held not to have changed since the fifth century, this would be evidence of the very early date at which the cult of the saints reached Rome.

We learn from Gregory of Tours that relics of the saints were brought to the Church of St. Martin of Tours from Rome in the sixth century and the cult of the twin saints spread gradually through Italy, France, Germany, and Spain, and by the end of the seventh century they were known in England. In later mediæval times the two saints became associated with medical corporations and especially with those of surgeons and barbers. Thus Cosmas and Damian came to take a prominent place in the record of the Companies of Barber Surgeons of London and York. In France the statutes of a confraternity of surgeons known as the brother-

hood of Saints Cosmas and Damian can be traced back to the middle of the thirteenth century.

Of the arrival of the cult of Saints Cosmas and Damian in Spain we learn something from verses written by St. Isidore of Seville (570–636) for the fourteen presses (*armaria*) of which his library was composed. These presses were adorned with the portraits of twenty-two authors, four of whom, Hippocrates, Galen, Cosmas, and Damian were physicians, and on the medical section was inscribed the following:

Quos claros orbe celebrat medicina magistros,
Hos præsens pictos signat imago viros.
Sunt medico dona, quandiu quisque laborat.
Æger jam surgit, nulla lagena venit.
Quod debes medico, redde æger, ne mala rursus
Occurrant, curret denuo nemo tibi.
Pauperis attendat medicus censum, atque potentis:
Dispar conditio dispari habenda modo est.
Si fuerit dives, sit justa occasio lucri;
Si pauper, merces sufficit una tibi.

That the cult of Cosmas and Damian entered the Spanish Ritual and survived the Moorish period is proved by the following prayer from the Mozarabic Liturgy printed by Cardinal Ximenes:

Deus, sanator noster & medicus sempiternus: qui Cosmam & Damianum inconcussa fide, insuperabiles in virtute fecisti: ut per suscepta vulnera vulneribus mederentur humanis. Qui ante passionem ex terreno medicamine, salutem operati essent in populis, hos, quæsumus, nostris infirmitatibus & custodes & medicos deputa. Per eos sanentur infirma. Per eos non recrudescant sanata. Per hos corpora, per hos animæ medicinam acquirant. Hi typicis animæ ægritudinibus finem, hi patulis celerem impendant ægrimoniis sanitatem. Hi putredines vulnerum orationibus defæcent. Hi manu precarionis abdita vulneratorum expurgent. Hi miseris humanis medelam inlaturi occurrant. Hi pressuris hominum concita levigatione subveniant. Hi etiam sic nos his a peccati morbo servent inlæsos, ut ad cælestem perducant patriam coronandos.

Perhaps the most attractive of the liturgical passages referring to Cosmas and Damian is a hymn that was in use at Minden.

It has been printed by Daniel in the "Thesaurus hymnologicus," and is as follows:

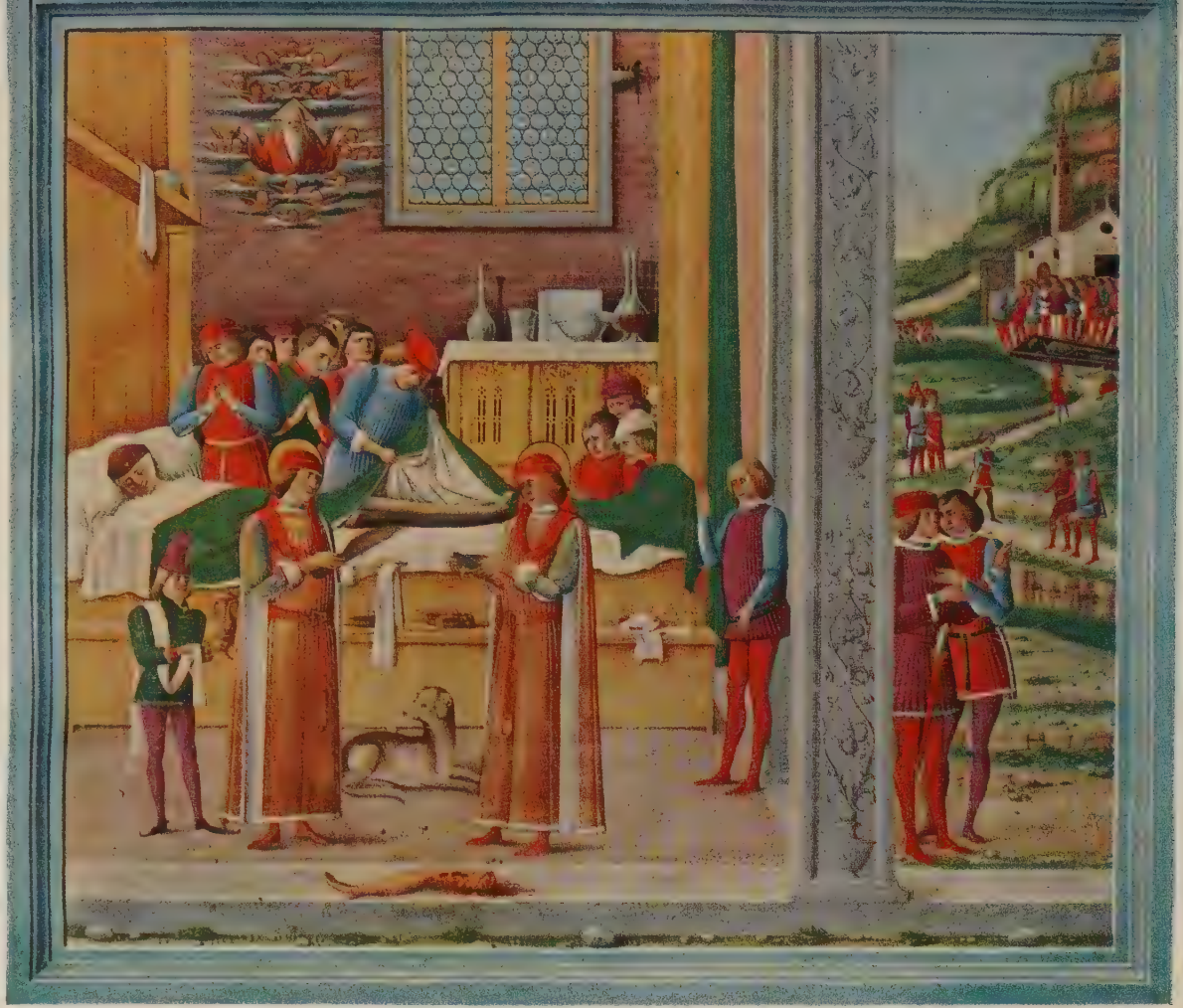
Cordis, oris symphonia
Triumphantum sub Lycia
Cosmæ & Damiani pia
Pangamus præconia:
  Quorum vita gloriosa
Pugna fortis & famosa
Mors felix & pretiosa
Sublimis victoria.

Arte docti medicinæ,
Dono gratiæ divinæ,
Sanitati repentinæ
Languidos restituunt:
  Ægrum curant & obsessum,
Gratus dant, gratis concessum,
Cæcis visum, claudis gressum,
Surdus opem tribuunt.

Victi, torti, carcerati,
Crucifixi, lapidati,
Sagittati, cruciati
Per tormenta varia:
  Ignem, aquam transierunt,
Ferro mortem pertulerunt,
Dulce mori sic duxerunt
Pro cælesti gloria.

O vernantes cæli flores,
Rosis rubicundiores,
Inclyti propugnatores
Fidei catholicæ:
  Optimates honorati,
Laureati, purpurati,
Nostri sitis advocati
Coram summo Judice.

The miracles of Cosmas and Damian have been favourite subjects with the makers of Byzantine icons in the East as well as with Renaissance artists in the West, where Fra Angelico, Bicci di



Lorenzo, Botticelli, Ghirlandajo, Fra Lippo Lippi, Matteo di Siena, Michelangelo, Juan Garcia de Miranda, Pesellino, Tintoretto, and Titian, among others, have been inspired by them. Fra Angelico especially has depicted the miracle of our miniature in a painting in the Galleria dell' Accademia delle belle Arte at Florence.

This story is one of the many legends of marvellous healing that have grown up around the names of Cosmas and Damian. It is told in the "Golden Legend" that a certain man, suffering with cancer of the leg, went to pray in the Church of Cosmas and Damian at Rome. When he had completed his devotions sleep fell upon him and he beheld in vision the twin saints by his side. One said, "What shall we do to replace this diseased leg when we have cut it off?" to which the other replied, "A Moor has just been buried in San Pietro in Vincole; let us take his leg for the purpose." Then they brought the dead man's leg and with it replaced the leg of the sick man. When the patient awoke he almost doubted whether it could be himself, but his neighbours, seeing him thus healed, looked into the Moor's tomb and found that there had indeed been a change of legs.

There are several representations of this particular miracle familiar to students of Renaissance Italian art, but that which we here render is almost unknown. It is in a magnificent Choir Book in the possession of the Society of Antiquaries in London and is one of a series representing the miracles of the two saints, and especially those connected with their death. The Choir Book came into the possession of the Society of Antiquaries by a bequest from the late Sir Thomas Brooke in 1908, and nothing is known of its history. At one place, there is an inscription in a later hand alleging in it that the miniatures are by Andrea and Francesco Mantegna, but this seems most unlikely. Nevertheless, it is quite evident that the miniature is the work of a master hand and is not, as is so commonly the case in manuscripts of this sort, an artisan product turned out to order.

In the MS. the miniature measures 10 inches by 9, so that our representation is reduced from the original by rather less than half the diameter. The condition of the picture is remarkably good. The scene is divided into two parts. On the left is an operation room, on the right an open air view of a hill and a group of buildings.

We may turn our attention first to the scene on the left. In the foreground stand the saints, who have completed their operation. Each has in his hand a surgical knife which he is wiping on a cloth. The saint on the left is attended by a page who bears a towel and a carafe of water for washing the hands. The attendant of the saint on the right has just drawn the curtain displaying the patient in bed. In the foreground lies the amputated cancerous leg, the ulcerous character of which is clearly discernible. A dog lies between the saints at the foot of the bed. On a ledge or step running along the side of the bed can be seen two cases of surgical instruments, one closed and one open, two pairs of forceps and some blood-stained cloths. The patient as he lies in bed is being examined by an admiring crowd, one of whom raises the coverlet to display the transplanted limb. The line of demarcation between the black skin and the white can be clearly discerned.

Especially worthy of notice is the expression on the face of the patient. It is that of a man recovering from a narcotic rather than of one rallying from shock or awakening from sleep. Those who have studied the records of mediæval medicine have often been struck by the drastic character of some of the operations undertaken, and it is difficult to believe that some sort of anæsthetic was not habitually used. This procedure is, indeed, seldom mentioned, but it appears probable that the number of records bears no relation to the frequency with which such measures were employed. The truth is that medical writings often omit the very commonest processes. Thus, references to the use of anæsthetics hardly find any place even in modern treatises of surgery, yet they are of universal application. So also it would appear that the use of narcotics was common enough in mediæval surgery, though the references to it are comparatively rare and meagre.

The figures standing around the bed are evidently portraits and are not without some features of medical interest. We would point especially to the middle figure in the front row of the group on the left. He stands in his green coat with clasped hands and eyes fixed with wonder on the transplanted limb. On the side of his scalp above the right ear are to be seen two white hairless linear areas. The position and form of these marks suggests that they are not the effects of some disease such as *Alopecia areata*, but are the

Enlarcement of the Central Portion of the Miniature.

Enlargement of Detail in Miniature, Showing Swallow's Nest with Mother Bird and Young.

result of the use of cautery in the temporal and parietal region. This is a remedy against headache often resorted to in the Middle Ages.

At the head of the bed and out of reach there hangs another towel and perhaps an ointment-pot. Against the brick wall at the end of the room there is a beautifully carved cupboard on the top of which stand some medical appliances. Here are four vases containing some liquids, a nest of basins, and a square glass vessel. Above and to the left is an Epiphany, the head of the Deity being surmounted by a triangle with the initials P. F. S. (Pater, Filius, Spiritus Sanctus) at the three corners. On the right of the window a swallow has made her nest and is tending her young. The extreme fineness and delicacy of the painter's work is well seen in the enlargement which we give of this beautiful little detail.

The scene to the right of the operation room is of somewhat inferior workmanship to the rest of the picture and is possibly in part by another hand. Various groups of less interest for our purpose are scattered through the scene. In the middle distance, however, and in front of a building that resembles the Church of San Pietro in Vincole there stands a crowd gazing in astonishment at an open coffin within which lies a one-legged black corpse. In front of the coffin can be seen a white amputated leg which bears trace of disease. The presence of this leg affords perhaps some evidence that this part of the painting is by another artist, since it raises to five the number of legs that have to be distributed between the two subjects of operation, an improbable number for two men even in the age of miracles.

So far as manuscript material is concerned this miniature is the finest we have encountered representing a surgical operation. We have to thank our friend Mr. Sidney Cockerell of the Fitzwilliam Museum at Cambridge for drawing our attention to it. To another friend, at once a priest and a physician, Father John Rory Fletcher, we are grateful for much information concerning the story of the saints and for many bibliographical references.

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This list of books makes no claim to completeness. To construct a comprehensive bibliography of these saints would be an enormous task.

We give only a selected list of more modern works, many of which themselves contain material for a larger bibliography.

I. *Cosmas and Damian in Art.*

Andrea Corsini, "Il Costume del Medico nelle pitture fiorentine del Rinascimento," Florence, 1912.

This beautifully illustrated little work contains reproductions of all the important representations of our saints in Florentine art. The Florentine pictures are of special importance as Cosmas and Damian were the patron saints of the Medici family.

Raymond Crawfurd, "Plague and Pestilence in Literature and Art," Oxford, 1914.

Contains numerous references to our Saints.

Anna Brownell Jameson, "Sacred and Legendary Art," London, 1848, and many subsequent editions.

A popular and well-tried compendium of its subject with some useful references to pictures and legends of Cosmas and Damian.

N. Bell, "The Saints in Christian Art," 3 vols., London, 1901–4.

An index of its subject.

It is impossible to give here a list of the numerous works of art representing our saints. There is one mosaic, however, that is of special importance on account of its great antiquity. It is in the church of Cosmas and Damian in the Forum at Rome and is very well rendered in colours by G. Battista de Rossi in his "Musaici Cristiani e Saggi dei Pavimenti delle Chiese di Roma," Fascicolo V. A good account of the Forum church itself is given by Leclercq in Châbrol's "Dictionnaire d'Archéologie crétienne."

The sole literature referring to the choir book from which our reproduction is taken is in the text associated with Plates 171–173 of the "Facsimiles of Ancient Manuscripts," Part VII, published by the New Palæographical Society, London, 1909.

The sole reason for attributing the illuminations to the Mantegnas is an inscription on folio 15 verso in a sixteenth century hand that runs as follows: "*Magister Andreas et Franciscus de Mantinea ornarunt cartas artibus egregus,*" followed by the words "*Frater Jacobus de Mantua propria manu.*" It is improbable that this attribution by Jacopo di Mantua is correct.

The style of our miniature indicates that it was executed in Northern Italy at the end of the fifteenth century. The character of the work is held to be suggestive of the school of Ferrara.

II. *Cosmas and Damian in Eastern Legend.*

The relation of the Eastern versions of the history of the saints to pre-Christian and pagan traditions is discussed in the following works:

L. Deubner, "De incubatione, capita quattuor," Leipzig, 1900.

H. Delehaye, "Synaxarium ecclesiæ Constantinopolitanæ," Brussels, 1902.

J. Rendel Harris, "The Dioscuri in Christian Legend," Cambridge, 1903.

Franchi de' Cavalieri, "I SS. Gervasio e Protasio sono una imitazione di Castore e Polluce?" in the *Nuovo Bulletino di Archeologia Cristiania*, IX, p. 109, Rome, 1903.

H. Delehaye, "Castor et Pollux dans les légendes hagiographiques," in the *Analecta Bollandiana*, XXIII, p. 427, Brussels, 1904.

Mary Hamilton, "Incubation, or the cure of Disease in Pagan Temples and Christian Churches," St. Andrews, 1906.

L. Deubner, "Kosmas und Damian," Leipzig, 1907.

W. E. Crum, "Place names in Deubner's Kosmas und Damian" in the *Proceedings of the Society of Biblical Archæology*, XXX, p. 129, London, 1908.

H. Delehaye, "Les Légendes grecques des Saints militaires," Paris, 1909.

It is interesting to compare with the Eastern legends the "Life of Apollonius of Tyana" by Philostratus, of which there is a convenient translation by F. C. Conybeare in the Loeb Library, London, 1912.

III. *Cosmas and Damian in Western Legend.*

The development of the Western legend has been less scientifically investigated than the Eastern. It may be followed in part in the following works:

de Smedt, "Acta Bollandiana," Vols. XXVII and XXX, contains much bibliographical material concerning Cosmas and Damian.

Jacobus de Voragine, "Legenda Aurea." A convenient edition is that by Graesse (1846). The story of our miniature is told on p. 639.

"Actes des Martyrs," published by the Bénédictins de la Congrégation de France, Vol. III.

Alphonse-Marie Fournier, "Notices sur les Saints Médécins," Solesme, 1893, contains copious bibliographical material. We have used this book considerably in our article.

H. Dauchez, "Les Armoiries des Chirurgiens de S. Côme aux XVI^e^, XVII^e^ et XVIII^e^ siècles," in the *Bulletin de la Société médicale de S. Luc, S. Côme et S. Damien*, VI, p. 37, Paris, 1900.

H. Dauchez, "Saint Luc, Saints Côme et Damien," in the *Bull. de la Soc. méd. de S. Luc, S. Côme et S. Damien*, VIII, p. 1, Paris, 1902.

H. Dauchez, "L'Église Saint Côme de Paris (1255–1836) et l'Amphithéâtre d'Anatomie de Saint-Côme (1669)," in the *Bull. de la Soc. méd. de S. Luc, S. Côme et S. Damien*, X, p. 1, Paris, 1904.

H. Delehaye, "Les Légendes hagiographiques," Brussels, 1905.

George L. Walton, "The Medical Saints Cosmo and Damian," in the *Proceedings of the Charaka Club*, IV, p. 15, New York, 1916.

Charles Green Cumston, "A Note on S. Cosmas and St. Damian, the Patron Saints of the Confraternity of Surgeons of France." *Proceedings of the Royal Society of Medicine (section of the History of Medicine)*, XI, p. 70, London, 1918.

Acta Sanctorum for Sept. 27th, Vol. VII, p. 100.

SOME SEVENTEENTH-CENTURY WRITINGS ON DISEASES OF CHILDREN

By George F. Still, M.D., London

SPECIAL attention was already being given to diseases of children when the seventeenth century opened. In 1604 Omnibonus Ferrarius, a physician of Verona, who modestly bestows upon himself the title of "Medicus et philosophus," produced a tiny volume of "aphorisms," "De Arte Medica Infantum."

From the time of Hippocrates, the promulgation of aphorisms had been a recognised mode of medical teaching, and the philosopher of Verona, a close follower of Hippocrates, no doubt was ambitious to emulate his master. In his preface he announces in somewhat florid terms his decision to publish to the world his aphorisms, "plucked as flowers from the fields and woven into golden garlands." His first "flower" is at any rate a choice one; it deals with the derivation of the word "puer." "Infans dicitur ille qui nondum fari coepit. Puer vero qui purus est et nondum ad pubertatis annos pervenit." Had the physician and philosopher been studying the "De Lingua Latina?" His etymology certainly savours of Varro with his "lucus, a non lucendo."

Ferrarius passes at once to the practical details of infant feeding, and it is particularly noticeable that he seems to take for granted that all infants must be breast-fed; the possibility of feeding with any other milk than human milk is not mentioned. The choice lay between maternal suckling and wet-nursing; the patent-food vendor was not yet darkening the infant horizon, nor was the purveyor of cow's milk replacing the natural food of infancy by a mixture of cow's milk, manure, and bacteria. But even in those days there was evidently a tendency to neglect the maternal duty of suckling, and Ferrarius thunders forth his indignation against the mother who delegates this function to another: "Inhumanum monstruosumque esse videtur filium concepisse et sine legitima causa eundem seorsum

alieno lacte nutrire," and again, "She who fails to suckle her own child is no proper mother."

At that time physicians seriously believed that the moral characteristics of the nurse were conveyed by the milk, a belief by no means extinct yet amongst the laity. Ferrarius in common with other writers of this period, uses this belief as a strong argument against the use of wet-nurses. In support of it, he affirms that kids fed on ewe's milk grow finer hair than normal, while lambs fed on goat's milk have an unusually coarse wool. His directions for the choice of a wet-nurse include the curious statement that "a woman makes the best nurse when she has had a male, not a female, child."

The second part of his aphorisms deals with the general management of the child from birth up to school age. Some of his pronouncements are as valid to-day as they were three hundred years ago, e.g., "Infantes nunquam ploraut sine legitima causa"; or this, which might be inscribed on the wall of every modern nursery, "Infans semper exactissimam munditiam amat," "an infant always wants the most scrupulous cleanliness."

His directions for weaning, however, suggest that the learned doctor was not altogether a trustworthy observer; he advises that an infant should be entirely breast-fed until the incisors are cut, and that weaning should take place when the infant has the full number of its teeth; the full number, he adds, is thirty-two! The educationalist of to-day might do well to ponder on the advice of Ferrarius that "schooling should not be begun before the age of six years."

Amid much, however, that is sound and practical, there lurks the superstition of his time. "The sign of the Blessed Cross," he says, "should be used to protect the infant, lest he be bewitched by some maleficent owl at night." In explanation he mentions in an apologetic manner, as if unable to deny it, "the widespread and old-standing belief in certain mysterious old women, popularly known as owls, who sucked the blood of infants, to renew their own youth."

The effect of environment on character has always been an interesting subject for speculation. How much Ferrarius appreciated it is evident in an aphorism which at first sight is puzzling. Amongst the influences which may spoil a child's character he mentions "consuetudines pravæ, cibi, potus, . . . et mala musica"! The

latter part refers presumably, not to the unchristianising influence of the itinerant German band, but to the μουσική which Plato and Aristotle had regarded as one of the three or four branches of education and culture, in the sense of artistic training.

The third part of Ferrarius' work deals with affections of childhood as distinct from infancy, and with treatment. He attaches much value to articles hung from the neck; "the tooth of a wolf," he says, "hung on an infant's neck, specially assists teething." "In the opinion of some," he says, "the tooth of a dead man hung on an infant's neck" has a similar value. For the prevention of digestive disorders in infancy, he recommends red coral hung from the neck—a prophylactic to which some mysterious value has been attached even in recent times. The cure of epilepsy is promised from the hanging of a peony root about the child's neck.

Omnibonus Ferrarius had published in 1577 a fuller work, "De Arte Medicina Infantium," of which at least one further edition was published in 1605.

He shews but little originality, and grounds much of his statement on Galen, Hippocrates, Avicenna, and Paulus Æginetus. His section on "inflatio capitis" is interesting as reflecting the prevailing ideas of the nature of hydrocephalus, and also perhaps as giving some clue to the origin of the term "external hydrocephalus," a condition which still prevails in text books, though it seems to prevail nowhere else, unless indeed a ruptured internal hydrocephalus, or the mere compensatory fluid which is found with a shrunken brain, e.g., with cortical sclerosis, is called by such a misleading name. Certainly the writers of that day attached no such significance to it.

Ferrarius divides "inflationem capitis" into three varieties: (1) "Ab aqua extra cranium; (2) ab aqua intra cranium; (3) inflatio capitis a flatu."

His description of the first variety, which by other writers of that period is alternately described as external hydrocephalus, shews clearly that he is referring to any fluid swelling on the outside of the skull, and includes caput succedaneum, cephalhæmatoma, and probably any suppuration beneath the scalp.

The third variety, he explains, is the κεφαλῆς ἐμφυσήματα of Greek writers, distension of the head with air—a serious condition apparently; he describes how it separates the sutures and "foras

erumpit"! no wonder the unlucky infant shewed "watchings, pains, and wailing."

In 1604 there appeared another work on children, Johannes Geckius, "De Puerorum Tuenda Valetudine Atque de Eorundem Morbis Profligandis." He describes himself as "Medicus Bononiensis" and his work as "a brief and complete guide, being a compilation of the views of Latin, Arabian, and Greek writers."

He starts from the cutting of the umbilical cord "acuto gladio," and, like Ferrarius, insists upon the duty of maternal suckling. "A mother," he says, "should regard it as no mean duty to give her breast to her infant." If a wet-nurse must be used, she should be "bonis moribus prædita, nam nutricis qualitates, et ad animum et ad corpus attinentes, contrahunt infantes lacte quo utuntur mediante."

Apart from the management of the infant, his book covers the usual range of subjects which seem to have been included at that time under "Diseases of Children," viz., smallpox and measles, fevers, some skin affections, particularly erysipelas and itch, and burns. This last subject is so constantly part of the contents that one must suppose that a burn was one of the commonest accidents of children in those days.

In 1609 there appeared in Paris a much more complete handbook on the diseases of children than either of those already described; the work of a Court physician, who apparently specialised in the practice of obstetrics as well as in the department of children; it was entitled, "De la Nourriture et Gouvernement des enfans, des le commencement de leur naissance: Et le moyen de les secourir et garentir des Maladies que leur peuvent survenir dés le ventre de leur mère et premier age. Par Jacques Guillemeau, Chirurgien a ordinaire du Roy et Juré a Paris." Paris, 1609. This work is bound up with another treatise by the same author, "De L'heureux Accouchement des Femmes."

He gives minute and admirable directions as to the care of the new-born infant. His explanation of the value of breast milk and maternal suckling is perhaps not intended to be taken literally. "Le plus expedient seroit que l'enfant fust nourry de sa propre mere, plus tost que d'une estrangere, pource que son laict qui n'est que le sang blanchy (duquel il a esté faict et nourry neuf mois au ventre de sa mere) lui sera tousiours plus familier et naturel que

celuy d'une autre femme. Si la propre mere le faict nourrir, elle sera appellee mere entière." There is something appealing in this final outburst, this promise of the crowning title of motherhood for her who suckles her infant, "She shall be called the complete mother."

The terms "rachitis" and "rickets" were then unknown, but Guillemeau not only recognised the occurrence of kyphosis and beading of the ribs, but also their dependence on faulty feeding. He insists upon the importance of giving only breast milk until the incisors are cut, "car de luy donner autre nourriture que le laict ou bouillie devant qu'il ait des dents, cela luy apporteroit quantite de cruditez et vent qui sont cause souvent (comme dit Avicenne) de luy faire des gibbositez et contusions a l'espine du dos et aux costez." On the authority of Paulus Æginetus and Avicenna he recommends weaning at two years, and considers that health is threatened by weaning before dentition is complete.

He deals with congenital deformities in addition to many of the common diseases of childhood. An operation in those days was not undertaken without due circumspection; he mentions a case of harelip over which a consultation was held and six of the consultants were against operation—we are not told how many were in favour; but the operation was done and the infant died. A consultation must have been a spacious affair in those days.

Hints on treatment gleaned from this period are not promising: enuresis is a disorder which lends itself to practical suggestions and one turns hopefully to the therapeutics of the past; but "a cock's crest dried and administered in the form of a powder," or "the brain of a hare steeped in wine," hardly carry conviction.

Like most writers of his day on diseases of children, he deals with smallpox and measles (which no doubt included a variety of rashes, infectious and otherwise) but unlike some of them he includes also the great pox, syphilis, which was evidently prevalent in France, and appears in some English books of the period as "the French pox."

In the middle of the seventeenth century there appeared a work which, though it deals only with one particular disease, may be regarded as the first important contribution to the study of diseases of children in this country, namely, "Glisson on the Rickets," a

work of which England may justly be proud. It marks a big step forward in the study of disease; its outstanding feature is careful clinical observation and combined therewith a scientific insight into the value of evidence: which makes one feel that given the wider knowledge of modern times, Glisson would have ranked amongst the foremost scientists of to-day. The contrast between his book and those other works which have been already described, is the contrast between mediæval ignorance and "sound learning."

The first edition was published in London in 1650; it was in Latin and entitled, "De rachitide, sive morbo puerili, qui vulgo 'The Rickets' dicitur; adscitis in operis societatem G. Bate et A. Regemortero. 8vo. Lond." In its original Latin form it passed through at least four editions, and within a year after its first appearance it was translated into English, as the title page of the 1651 edition shews:

"A Treatise of the Rickets: Being a Diseas common to Children. Wherein (among many other things) is shewed, 1. The Essence. 2. The Causes. 3. The Signs. 4. The Remedies of the Diseas. Published in Latin by Francis Glisson, George Bate, And Ahasuerus Regemorter; Doctors in Physick and Fellows of the Colledg of Physitians at London. Translated into English by Phil. Armin. London: Printed by Peter Cole, at the sign of the Printing-Press, in Cornhil, near the Royal Exchange, 1651."

The preface explains to the "Courteous Reader" that this book was the outcome of papers contributed by various observers "in privat meetings (which som of us Physitians use sometimes to have for Exercise-sake in the works of Art)." It is pleasant to think of the little coterie, consisting of eight fellows of the Royal College of Physicians, whose names are preserved in the preface, who met together to discuss rickets in 1645, close on 130 years before the foundation of the oldest existing medical society in England.

At length they decided to publish their conclusions in the form of a joint treatise, and Dr. Glisson, Dr. Bate, and Dr. Regemorter were chosen to carry out the task. It was found, however, that Glisson's contribution was so important and original that it was thought best he should undertake the work alone, which he consented to do, if his two intended colleagues would consent to help him with their criticism and judgment. "And so at the length we have brought this

work (such as it is) to perfection and have offered it to the publick view, being by no means moved thereunto by an itch of writing (which is the Epidemical ill custom of this age) but by this Consideration only, That becaus we are not born for our selvs, we might make these (such as they are) common, which in som measure may advance the health of Infancy and tender age (in which for the present a great part of Mankind, but for the future all Mankind is comprehended) and likewise propagate an Encreas unto Learning." Surely a not unworthy preface to a fine piece of work.

Glisson affirms that rickets

"Is absolutely a new Disease and never described by any of the Ancient or Modern Writers in their practical Books, which are extant at this day, of the Diseases of Infants. . . . This Disease became first known (as neer as we could gather from the Relation of others after a sedulous enquiry) about thirty years since, in the Counties of Dorset and Somerset, lying in the Western part of England; since which time the observation of it hath been derived into other places, as London, Oxford, Cambridge, and almost all the Southern and Western parts of the Kingdom: in the Northern Counties this affect is very rarely seen and scarcely yet made known enough among the Vulgar sort of people. The most receaved and ordinary Name of this Disease, is The Rickets: But who baptiz'd it, and upon what occasion or for what reason, or whether by chance or advice it was so named, is very uncertain."

Apparently Glisson and his collaborators felt that the dignity of Medicine required something less homely in the way of nomenclature, and

"Because they which are expert in the Greek and Latin tongues may peradventure expect a Name from us whereof some kind of Reason may be given, we have made fit together divers Names in this Disease. . . . One of us by chance fell upon a Name which was complacenceous to himself and afterwards pleasing to the rest: now this was *νόσος* *ῥαχῖτις* or indeed *ῥαχίτης* . . . the Spinal Disease . . . for the Spine of the Back is the first and principal among the parts affected in this evil."

Glisson starts with an admirable chapter on "Anatomical observations collected from the Dissection and Inspection of Bodies subdued and killed by this Disease." His record of the external and internal appearances is a model of careful post-mortem investigation;

the more praiseworthy in view of the state of medical knowledge at the time. His scientific insight and judgment are well shewn in two cautions which he gives to the Reader:

"That the dead Bodies which we opened were most vehemently afflicted with this Disease whilest they were animated, for they are supposed for the most part to have yeelded to the very magnitude of the Disease, and therefore we must not expect that magnitude of the Affect or Symptoms which we here describe, in other Bodies yet living or newly besieged . . . that almost all Diseases in processe of time, do unite unto themselves other affects of a different kind and therefore that Chronical Diseases are for the most part complicated before death; Let them not therefore imagine that every preternatural thing that is found in dead Bodies though destroyed by this affect must of necessity belong to this evil."

In his consideration of the causes of rickets Glisson naturally shews the limitations of a time when physiology was scarcely more than in embryo, when the Animal Spirits generated in the brain, rushed backwards and forward "by a rapid and sudden motion like lightening" in flux and reflux through the spinal marrow nerves; and the Vital Spirits were excited or generated within the ventricles of the heart.

Glisson recognised the association of scurvy with rickets, and was in advance even of some writers of our own day in realising that there is no essential connection between these two diseases. He writes:

"The Scurvy is sometimes conjoyned with this Affect. It is either hereditary or perhaps in so tender a Constitution contracted by infection, or lastly it is produced from the indiscreet and erroneous Regiment of the infant and chiefly from the inclemency of the Ayr and Climat where the Child is educated. For it scarce holdeth any greater commerce with this Diseas than with other Diseases of longer continuance."

His description of infantile scurvy is noteworthy:

"The Scurvy complicated with this affect hath these signs: (1) They that labor under this affect do impatiently endure Purgations; but they who are only affected with the Rachites do easily tolerate the same. (2) They are much offended with violent exercise, neither can they at all endure them. But although in this affect alone ther be a kind of sloth-

fulness and aversation from exercise, yet exercise doth not so manifestly, at least not altogether so manifestly hurt them, as when the Scurvy is conjoyned with the Rachites. (3) Upon any concitated and vehement motion they draw not breath without much difficulty, they are vexed with divers pains running through their joynts and these they give warning of by their crying, the motion of the Puls is frequent and unequal, and sometimes they are troubled with a palpitation of the Heart, or threatened with a Lypothymie, which Affects are for the most part soon mitigated or altogether appeased by laying them down to the rest. (4) Tumors do very commonly appear in the Gums. (5) The urin upon the absence of the accustomed Feaver is much more intens and encreased."

It may be doubted whether Glisson is really describing here infantile scurvy as we know it now, an affection chiefly of the latter half of the first year, especially the seventh to the ninth month, for it is evident from other writers of this period, some of whom have already been mentioned, that breast feeding, which is a most potent preventive of scurvy, was practically universal and was continued later than it is at the present day. Moreover, it was particularly noted by Glisson that rickets hardly occurred under the age of nine months, and reached its maximum intensity from eighteen months to 2½ years of age, so that when he writes of "Scurvy conjoyned with the Rachites," he is evidently dealing with scurvy of a later age than that of the infantile scurvy of modern text books.

Scurvy was apparently rife in the seventeenth century, and treatise after treatise appeared at that time dealing with the disease in adults, some of these, e.g., Eugalenus, "De Morbo Scorbuto," Hagae, 1658, and Balthazar Bruno, "De Scorbuto Tractatus," 1658, particularly mention the occurrence of scurvy in children. The latter says that the gum symptoms are more common in children than the pains in the legs, but in none does there appear any description of the disease in the infant (Eugalenus mentions an infant as having had scurvy because it had a convulsion whilst being fed by a scorbutic mother—but with no better evidence).

Glisson devotes several chapters to treatment, but here, as in his pathology, there is so much wordy generalisation on principles that it is difficult to separate the wheat from the chaff; for instance, he devotes pages to discussing the duties of a physician in regard to palliative, as opposed to curative, treatment of disease in general,

before he comes to a lengthy consideration of the various theoretical indications, "curative, preservative, and conservative." At last he reaches the practical aspect of treatment and deals first with the surgical part, "The Chirurgical (methods) commonly received and approved in this Affect and famous above the rest are chiefly two: Scarification of the Ears, and little Fountains or Issues." He gives anatomical reasons for the blood-letting from the ear, which he considered of some value: but he adds:

"It seems to be ridiculous and superstitious which some are busie about when they administer this Scarification; whilst they fasten the Blood of the right Ear suck'd up into Wool to the left Hypochondry and the Blood of the left to the right. Thus much of Scarification."

"Issues in this Diseas are much approved and we have known some Children cured only by the help of this means. . . . It is a powerful remedy against the Hydrocephalus . . . and lastly to repress the inordinate encreas of the Bones. Also it manifestly drieth up the too much humidity of the Spinal Marrow, exciteth heat, strengthens the Nerves, and expelleth the astonishment."

The issue or fountain was a small ulcer, which he says should be made between "the Second and Third turning Joynt of the Neck," and was produced either by cautery, or by a small incision "with a sharp penknife," the cut being kept open by insertion of a pea or some foreign body.

He gives a large number of prescriptions, mostly complicated herbal mixtures, some containing eight or nine ingredients.

In 1659 there appeared a small text book of diseases of children by James Primrose, part of whose title to fame is the unenviable distinction of having, in his earlier days, poured doubt upon the observations of Harvey. In 1655 he had also published a work on diseases of women.

In his work "De Morbis Puerorum," printed in Rotterdam, he shows no special originality, indeed, rather a slavish following of earlier writers, Hippocrates and Galen, Rhazes and Paulus Æginetus, sometimes with acknowledgment and sometimes without. Some of his directions for the care of infants are curious: he advises, amongst the substances which may be used for the washing of the skin of the new-born infant, the child's own urine. If an infant is specially

feeble at birth, a girl (virginem quandam) should first chew some aromatic herb and then breathe into his mouth—the infant should not be carried about "a sordidis vetulis quæ tetrum spirant odorem" (by dirty old women with stinking breath), peradventure a common type of the domestic nurse of the day, and not altogether unknown in our own.

The time of weaning he thinks may be chosen partly according to the phase of the moon, it is better to wean when the moon is waxing than when it is waning.

His book is divided into two parts, the first dealing with the general management of children, especially of the newborn infant, the second dealing with their diseases. In the latter he covers a large number of the affections of childhood in small space, thanks to the simplicity of pathology at that time: paralysis, for instance, "may occur in one limb or the whole body, and rises from thick humour"; with this satisfying summary of the varieties, etiology, and pathology of paralysis, he passes on to treatment.

Crying in moderate degree, he says, is not bad for children, it purges the brain—this dark saying being explained by a subsequent statement that "tears are serous humours transmitted to the eyes from the brain!"

On teething Primrose has much to say: rapid teething gives little pain but weak teeth; slow teething much pain and strong teeth. Teething is easier in spring and summer than in winter, a view which he is at much pain to reconcile with the dictum of Hippocrates, that teething is easiest in winter. His common sense, however, rebels here, as it does at times elsewhere, against tradition, and he demolishes the whole influence of season on dentition by an outburst of protest that seasons of the year have no power whatever to counteract the effect of a child's constitution in determining the ease or difficulty of dentition!

So, too, whilst he feels bound to include in his list of prophylactics various articles to be hung from the neck, a jasper, the tooth of a dog, the tooth of a wolf, and so forth, he adds as a cautious expression of personal opinion "quæ superstitiosa mihi videntur." Under the head of "Macies," the marasmus of modern text books, whilst referring to the supposed influence of witches and the evil eye, he declines to believe in any special power of witches, but thinks the

child's wasting may be the work of the devil. He gives a long list of things which, if worn round the neck or otherwise, were supposed to avert evil spirits, etc., but finally dismisses them all as an absurdity, and says: "Who can believe that any devil can be affected in the least by any one of these things or by all of them together?"

His last section is "De Morbo puerili quem in Anglia vocant Ricketts." He says that he first heard it called "Ricketts" in the town of Southampton in 1628, and that he saw it the same year in Yorkshire, where that name was then unknown. He says "the children of the country folk are rarely affected; but almost exclusively those of the upper classes and town dwellers because these are more luxuriously brought up." He follows Glisson so closely that one cannot but feel that he borrowed liberally from him with scant acknowledgment. "De hoc morbo," he says, "scripsit Medicus Londinensis-propterea paucissima scribam." He makes frequent references to Hippocrates and Galen, assuming that their remarks on the "spina quæ in gibbum attollitur" refer to rickets, whereas the context, in some parts at least, makes it almost certain that the condition they mention is spinal caries.

He condemns the common treatment of rickets by bleeding, which for this disease was done behind the ear: he says "scarcely was a name given to the disease in England before women contrived as a remedy, without reason or experience, bleeding behind the ears, a practice followed subsequently by physicians, but why I know not."

A sound piece of criticism not altogether out of date to-day is offered finally to the orthopædic surgeon.

> "Children often at the age of two years, when they begin to walk become bowlegged, and the Mother being anxious about it, seeks advice 'a Chirurgis, qui plerumque variis machinis crura et tibias erigere conantur, sed frustra, quia sponte naturæ, utplurimum circa ætatem trium aut quatuor annorum, tibiæ et musculi firmantur et partes ad naturalem statum redeunt.' "

The time is not yet past when the unfortunate rachitic child is laden "variis machinis": which in many a case could be discarded with advantage, if only parents would be persuaded that with proper care "circa ætatem trium aut quatuor annorum partes ad naturalem statum redeunt."

Primrose ends his remarks on rickets and his book with an anonymous recognition of Glisson's work, "Verum qui de hoc morbo plura voluerit Legat Librum Medicorum trium Londinensium, de rachitide."

This book is, indeed, a useful little summary of the subject of diseases of children, but betrays little or no original observation. Perhaps Primrose still regarded the production of medical books rather as an intellectual amusement than as a serious effort to promote the increase of scientific knowledge, as he had admitted was his wont twenty years earlier, when he published his attack on Harvey's discoveries: "a me scripta sunt γυμναστικῶς ad ingenii exercitium et oblectamentum, ut cætera soleo."

In 1680 Franciscus de le Boë Sylvius, Professor of the Practice of Medicine in Leyden, published a large work, covering the whole field of medicine, and he included in it (Praxeos Medicæ Appendix Tractatus I) a Treatise "De Morbis Infantium": the scope of which can be seen from the heading of the Chapters:

I. De Ictero. II. De ventris torminibus. III. De alvi dejectione viridescente acidumque redolente. IV. De singultu, nausea, cardialgia et vomitu ac præsertim Lactis coagulati. V. De aphthis. VI. De insultibus Epilepticis. VII. De Dentitione difficili. VIII. De Tinea et Scabie fera. IX. De Variolis et Morbillis. X. De Vermibus.

This treatise is frequently quoted by subsequent writers on diseases of children; and is a careful survey with some evidence of personal observation. In his treatment of infants Sylvius is said to have been such a constant prescriber of opium, that he was known as Doctor Opiatus.

In England none of the writers already mentioned obtained such vogue in the seventeenth century as Walter Harris. Born in 1647, he became Physician in Ordinary to Charles II in 1683, and six years later published his little book "De Morbis Acutis Infantum." It seems to have become the standard text book of the period, and remained so for about fifty years. First published in 1689, it went through many editions, and in English translations it was included as late as 1742 in J. Martyn's "A Full View of all the Diseases Incident to Children."

Harris uses the terms infancy to cover the first four years of

life, and childhood as extending to the fourteenth year. Like most of the previously mentioned writers, he deplores the refusal of mothers to suckle their infants, and it is interesting that amongst the reasons assigned are theatre-going and card-parties. He describes the drunkenness and depravity of the wet-nurse and the consequent fearful mortality amongst infants. He tells how the monthly nurses —in this period anterior to Mrs. Gamp—gave wine or spirit sweetened with sugar to the new-born infant to quiet its crying.

His description of colic and indigestion in infancy is excellent: the picturesque and at times almost conversational character of his writing probably accounts in no small degree for the favour which his book found.

Harris regards acidity as the one common cause of all infantile disorders; following in this view Franciscus de le Boë Sylvius.

In treatment he recommends the use of bleeding even for infants, for whom it is generally unsuitable, for spasmodic cough, for cough associated with a sudden rise of temperature, and in a bout of convulsions. He insists upon the value of purging, especially in febrile conditions, though he is at pains to shew that the strong cathartics recommended by Hippocrates are unsuitable for infants.

The use of opium in disorders of infancy he forbids altogether, except in the case of persistent vomiting. His book makes no pretence at system, it covers only a few of the diseases of childhood, and those but briefly, and the main portion of the work is followed by a series of case notes, in which the distinguished rank of his patients seems to be somewhat unnecessarily prominent, thus: "Nobilissimus infans filius natu maximus Illustrissimi Marchionis," etc., or thus: "Unicus filius illustrissimi Comitis," etc., or thus: "Honoratissima et unica Filia Serenissimi Principis ac Ducis, vix unum mensem adhuc nata," etc.

Indeed one may suspect that Harris was not altogether free from vanity: a suspicion rather strengthened by the opening remarks in one of his later editions, where he quotes verbatim a letter which he had received from Sydenham, who wrote, "I never flatter anyone, and I say it without any compliment, you are the first I ever envied. It is my sincere opinion, that this little book may be of greater service to mankind than all I ever wrote."

Posterity has not confirmed the high opinion which Sydenham expressed of Harris's work.

Sydenham himself can hardly be passed over in any survey of the writers on diseases of children in the seventeenth century, for though he did not profess to deal particularly with this subject, he nevertheless contributed at least one description, which made his name memorable in connection with children's diseases, as the term "Sydenham's chorea" still testifies.

In 1696 a translation from the original Latin of the work of "that excellent Practical Physician, Dr. Thomas Sydenham," was published by "John Pechy, M.D., of the College of Physicians in London," and from this the description of chorea is taken:

"In some kinds of Diseases of the nerves, both Bleeding and Purging do not only not do hurt but are necessarily prescribed: of which I will produce an Experiment I made, in a certain kind of Convulsion, which is vulgarly called Chorea Sancti Viti, of which Disease I cured no less than five by Bleeding and Purging by Intervals: of which sort of Disease I will speak somewhat, seeing it occurs opportunely, and evidently confirms the truth of what I have now asserted.

"Chorea Sancti Viti is a sort of Convulsion which chiefly invades Boys and Girls from ten years of Age to Puberty. First it shews itself by a certain Lameness or rather Instability of one of the Legs, which the Patient drags after him like a Fool; afterward it appears in the hand of the same side; which he that is affected with this Disease can by no means keep in the same Posture for one moment, if it be brought to the Breast or any other Part, but it will be distorted to another Position or Place by a certain Convulsion, let the Patient do what he can.

"If a cup of Drink be put into his Hand he represents a thousand Gestures like Juglers, before he brings it to his mouth; for whereas he cannot carry it to his mouth in a Right line, his hand being drawn hither and thither by the Convulsion, he turns it about for some time till at length happily reaching his Lips, he flings it suddenly into his mouth and drinks it greedily as if the poor Wretch, designed only to make Sport. For as much as this Disease seems to me to proceed from some Humours rushing in upon the nerves which provoke such preternatural Motions, I think the curative Indications are first to be directed to the lessening of those Humours by Bleeding and Purging, and then to the strengthening of the Genus Nervosum."

THE ENDOWMENT OF RESEARCH

By Arthur Thomson,

Professor of Anatomy, University of Oxford

THE endowment of research is a catch phrase which is very much misunderstood by the public. The prevailing idea seems to be that in proportion as you feed the mill with money so you will obtain results. The problem, however, is much more complex. The term Research is an unfortunate one, implying, according to its dictionary meaning, "careful search, diligent examination or investigation," a definition which seems to emphasise the laborious nature of the undertaking, but fails to bring out the fact that what is most desired is the genius, originality, critical acumen, call it what you will, essential for the utilisation of the data and the interpretation of their meaning.

For one man who will produce work of a really illuminating kind, there will be found many who turn out bulky records of observations or masses of data, from which, however, they are incapable of drawing any deductions. This failure to obtain any definite result for the work done may be due to two causes—either the unsuitability of the facts observed, or the inability on the part of the recorder to interpret them. In both cases the onus of blame rests with the researcher. In the first instance he proceeds to the collection of details the bearings of which may have no relation to the problem involved. Such data are often collected haphazard, with no real appreciation of their value or underlying significance. Proof of this is abundantly evident in many of the measurements recorded by physical anthropologists, where from lack of a guiding principle in their selection, much confusion has resulted in their interpretation. It follows, therefore, that the duty of everyone starting an enquiry is to be assured first of the applicability of the data involved to the end in view. Herein lies the germ of future success, and it is in this respect that the man with the true research instinct sees far ahead, and adapts the means to the end.

The collection of suitable data and their interpretation, whilst essential in all research, need not of necessity be the outcome of one man's work. Many men, though competent to do the spade work, yet fail to "see the wood for the trees." It is reserved for the few possessed of the higher research instinct to interpret the results. This difference in the nature of the work is too often overlooked when a man is appointed to do research work; it is assumed that he is competent to turn out results of the two types indicated.

The enlightened researcher, like the poet, is born, not made. He pursues his studies with no other desire than to ascertain the truth. To a man of such gifts, the mere accumulation of detail and the analysis of data are often a soul-destroying experience; his abilities are too valuable to waste in the preliminary investigations connected with his work. At the same time, it is necessarily admitted that he must have a training in the technique and processes of the class of work he is undertaking, so that he may direct the methods employed, varying them and inventing new ones as occasion may demand. If this be granted, then we are in a position to advance a stage in the manner in which research should be conducted.

Owing, as I think, to the undue emphasis now so often laid on "original work," a brilliant undergraduate, who by pure powers of receptivity has won distinction in the schools, is often awarded a Research Scholarship or Fellowship. In order to obtain promotion in the profession he may adopt, he feels it incumbent on him to do some "original work." The results are often more painstaking than illuminating; he may lack that originality and imagination, that constructive and analytical type of mind which is so essential to raise him to the level of the researcher of the higher type. He pursues his laborious and somewhat mechanical studies, oftentimes without being able to appreciate their significance; his work is, or may be, valuable to others, but out of it he gets little "kudos" himself.

Such experience, however, is not without its educative value. It has brought him into touch with a diversity of methods and technique, it has involved a fuller acquaintance with the literature of the subject he is investigating, it has trained him in the best way of marshalling his facts. This instruction is of necessity an essential in the training of anyone who aspires to be a researcher;

it fails only because there is no known educational means whereby one may imbue a man with mental gifts which he does not already possess.

For these reasons it seems that the promotion of research can best be accomplished by a due recognition of these facts. The discovery of the researcher most desired is not necessarily to be attained by educational means, though possibly in the process he may be found. The practical bearing of the problem at once brings us to the consideration of those aspects of the question which are educative and instructional.

As presented to the biologist—and it is only in this connexion that I venture to speak—the first essential is the adequate equipment of any institution which is associated with research. This is usually a costly business; too frequently, I fear, money is needlessly spent in the acquisition of apparatus which is never used. I have often been struck with the fact that whilst such appliances have often been ostentatiously displayed, when evidence of their use was asked for the results were not forthcoming. It is remarkable how some of those most distinguished in research have attained their results by means less costly, but indicative of more originality and inventive genius directed towards the end desired. The good research laboratory is a mine of wealth—the sham good laboratory is often a fraud. The best workman often uses the fewest tools.

Reduced to fundamentals, the essential fact emerges that a research laboratory must be under the care and direction of a man who is himself a researcher, who knows what should be done, and how to do it. Under his direction the man who aspires to be a researcher should pass something akin to an apprenticeship, thereby acquiring, under expert teachers, all the knowledge that is desired as to the collection, conservation, preparation, utilisation, and illustration of the different kinds of material he may be called upon to use. After having acquired a sufficient knowledge of this technique, the pupils so instructed might be utilised to assist the more advanced researchers, or it may be the Director himself, in the acquisition of those details which are so essential to the work in view.

Such an arrangement would have a two-fold benefit. It would afford a means whereby the pupils were provided with the oppor-

tunity of applying their technical knowledge to some practical purpose; they would be enlightened thereby as to the need of varying their methods in application to particular cases; they would be trained in the necessity of concentrating their minds on the one particular end in view; they would be led to recognise that for that purpose it was often necessary to avoid excursions into matters outside the enquiry, although such an experience might often provide suggestions for future investigation. Withal they would have the advantage of working with one who had already gained experience, and knew how the object in view could best be attained.

To the advanced researcher such assistance would be invaluable. He would be rid of the loss of time involved in the hardening, cutting, and staining of his tissues; he could avail himself of the services of these assistants in the preparation of his illustrations, graphic, photographic, or photomicrographic. Under his direction the pupil researcher could prepare such graphs, tables, or summaries as he thought desirable, and more or less uninterrupted time would be allowed him for the consideration of those conclusions towards which he was striving. No less important would be the assistance which might be rendered by the Juniors in preparing suitable abstracts from the literature concerned. Here the guidance of the Senior would be helpful and instructive, whilst at the same time much precious time might be saved on the part of the Senior in poring over the pages of endless monographs, many of which are more remarkable for their bulk than for their contribution to knowledge.

It would almost appear from the above that the division of labour as between the Junior and the Senior was unfair: it may be pointed out, however, that the Senior is responsible for the whole, and that the "spade-work" can be distributed among a number of Juniors. What is suggested is that the Senior should be relieved of that class of work which is purely technical, mechanical, or secretarial, and that he should supply the brains. It is a method which is adopted in many other forms of human activity. Why should it not be more frequently employed to further the interest we have most at heart? It is often said: "Oh, So-and-so did the work and the 'Chief' takes the credit." Let there be credit and due recog-

nition where credit is due, but the man with the idea, who finds the ways and means to carry it out, is surely the man who deserves the praise. He can afford to be generous to those who helped.

Now if such a system as this were carried out, besides saving an immense amount of time in the production of high-class research, it would provide abundant opportunities for enabling those best qualified to judge, easily to discriminate between those who are likely to become able researchers and those who have no gifts in that direction. The mere attainment of high technical skill, or a capacity for the laborious collection of undigested data, whilst admittedly an advantage, one might almost say an essential, in research, is yet no guarantee that those employed are endowed with the mental attributes that go to make the researcher. The one is the craftsman, the other is the artist.

It is from the Junior class that the Senior researchers should be recruited. Having, so to speak, served their apprenticeship, those of them who show the necessary qualifications should be encouraged and assisted in every possible way. It is for such as have proved their capacity that the financial endowments should be reserved, for oftentimes they are embarking on a career holding but little prospect of pecuniary gain. Such men may, and often do, lack the qualities which make successful teachers; all the more need, then, that they should be helped financially, and liberally endowed to enable them to continue, free from worry and care, the all-necessary and illuminating work they are engaged in. Such men, as a rule, have a higher ideal than mere greed of gain, they are not the class of men who are tempted to work for degrees. They rise superior to such considerations, and are prepared to stand or fall by their record. By their works shall they be judged.

For this reason I confess I am suspicious of all so-called "Research Degrees." The seekers after these distinctions, if such they may be called, are in most instances influenced by a desire to acquire an educational asset which may be of some advantage to them. The public are to some extent to blame for this, for unless a man can dub himself Doctor of this, that, or the other, the public are not likely to take him at his own valuation. An ordinary, or Honours, degree is usually a proof that a man has attained a certain standard of education in some branch of knowledge, be it cultural

or instructional. The possession of a research degree is merely proof that he has done a bit of work which has passed muster for the time being. He may never pursue his studies further; he may have none of the true spirit of the researcher, and may be content ever after to rest on his laurels. He has got what he wanted, and is now only concerned with how he can use it to the best advantage. For these reasons I am in favour of such degrees being honorary, the award being based on a man's record rather than on the accomplishment of one set piece of work.

The practical outcome of these considerations appears to point to the necessity for a revision of the generally accepted views with regard to research.

The recent policy of those directing the Honour School of Chemistry in the University of Oxford is one which deserves wider acceptance, and application to other subjects. By the terms of the Statute the candidate for the Honours degree is required to pass an examination in two parts. The *first* part demands an all round acquaintance with (1) Inorganic Chemistry, (2) Organic Chemistry, and (3) General and Physical Chemistry. The *second* part requires that he shall present records of experimental observations carried out under the supervision of an approved person. On this work the candidate may be subjected to a further examination in writing or viva voce.

The scheme provides some guarantee that the man who takes a science degree in chemistry leaves the university with the training necessary to equip him for research, an all-important matter when one realises how many will be the openings available for such men in connection with industrial firms in which research along chemical lines is of paramount importance. Further, the plan has this advantage, that in the necessary training of these men for their degree the opportunity is afforded of asking them to do pieces of work which may be helpful in the production of, or verification of, the results of others. It has also the advantage of enabling those engaged in research to reap the benefit of a "team" system, the need for which is becoming every day more recognised.

A more general adoption, in the Science schools, of the principle operative in the Honour School of Chemistry as outlined above, would do much to help in the selection of those best qualified to

undertake research, and would serve as a means of distinguishing those whose knowledge of their subject is purely cultural, from those who realise the bearing of the information they have acquired on the many questions still in dispute.

Failing the more general application of such an educational policy to other branches of science, it seems important that some means should meanwhile be provided to train the researcher. This has in most instances been attempted by encouraging the candidate to take a research degree. It is not always easy to guarantee that the candidate is qualified to carry out the research which he proposes to engage in, nor is it easy to deny him the degree if he has spent much time and labour without any adequate results. Anyone with experience of this kind of work knows that lines of enquiry which seem likely to lead to definite conclusions often fail to be productive of a satisfactory issue. In such cases, it is hard to penalise the candidate for his failure or negative result. He may not have been so fortunate in his choice of a subject as his fellow research students.

For a man who has not undergone any training in research, it would appear advantageous that he should acquire a knowledge of the essentials to equip him for the research he has in view. This might be done by the provision of financial help in the form of Scholarships and Exhibitions, together with access to a department in which he can obtain every facility for instructing himself in the necessary details under the supervision of qualified teachers. During the tenure of his Scholarship he might be utilised by those in charge to assist in the production of the work of the Senior researchers. Should he prove efficient and win the approval of those concerned, it would then be reasonable to provide him with a certificate—I hesitate to say degree—stating that he is qualified to undertake research. As the result of this preliminary training there would then be a reliable class of graduates from whom to choose, when it came to be a question of the disbursement of Endowments for that purpose, or the awarding of Research Fellowships. The men so selected could in their turn rely on the assistance of the students training for research in the laboratory in which the work was to be done. Time and money would thereby be saved, and by this co-ordination of resources possibly better and more extended enquiries might be undertaken.

Put briefly, the proposal has the advantage that the Researcher proper and those training for research combine forces, the former availing himself of the assistance of the latter; whilst the man being trained has the benefit of the direction of his Senior and acquires a practical experience of the many difficulties that may beset the investigation. The one teaches whilst being helped, the other helps whilst being taught, a combination which has all the advantages of "team work," yet reduces considerably the expense involved in carrying out the latter method.

GALEN, PLATO, AND IMMORTALITY

By E. T. Withington, M.A., M.B., Oxford

GALEN is a unique figure in history, a man who, though hardly attaining the front rank of genius, by his ability, diligence, and systematising power, aided by self-confidence and the opportunity of his time, acquired the dictatorship of a great profession, and gave laws to the civilised world in anatomy, physiology, and the doctrine and treatment of disease for thirteen hundred years. So much so that he became a synonym for medicine, and deserved that title far more than did the Roman Emperor who gave his name to another great profession—*Dat Galenus opes, sed Justinianus honorem.* But while "Justinian" is still read in the schools of law, the twenty-two volumes of Kühn's "Galen" are rarely disturbed even on the shelves of "learned" libraries, and, with one exception, will seldom show signs of having been read through since they were bound. The exception is volume five, which will often betray marks of frequent use, and will be found to contain a long treatise "On the Opinions of Hippocrates and Plato," a rich mine for searchers after philosophic fragments.

We should naturally class Galen with the Aristotelians rather than with the Platonists, and his spiritual home is doubtless among the former. But Aristotle, though usually mentioned with reverence, had committed an unpardonable error. He made the heart the seat of the soul and of all sensation, and looked upon the brain as little better than a cold damp sponge; whereas Plato's views might, with some little effort, be shown to be in accordance with, and perhaps derived from, those of Hippocrates. Galen therefore calls him repeatedly "the divine Plato"[1] and "first of all the philosophers,"[2] and quotes him verbally eighty-seven times, besides a multitude of casual references. About half of these are to the Timæus, upon which we have a fragment of a commentary, and nearly a third deal with the nature of the soul.

[1] 10.772. [2] 5.319.

But the treatise "On the Opinions of Hippocrates and Plato" corresponds to its title in the last two books only; the first seven might more appropriately be called "The Absurdities of Chrysippus," which form its chief attraction for the learned world. That great stoic, "The Pillar of the Porch," laid himself open to his enemies by writing more than 700 treatises now lost, but doubtless containing more absurdities than those attacked by Galen, which are, (1) the doctrine that the soul has its seat in the heart, (2) that it has only one "faculty," the so-called emotions and appetites being merely false or true judgments,[3] (3) that beings without judgment or reason, such as animals or young children, are soulless automata. This, says Galen, proves him and his stoic followers to be sophists in impudent opposition to the common sense of mankind.[4]

Aristotle and Posidonius, though they put the soul in the heart, at least admitted that it has several distinct faculties; but the correct view is that of Plato, who taught that the soul is of three kinds, rational in the brain, emotional in the heart, and appetitive in the liver, a doctrine partly derived from Hippocrates.

Plato teaches this both figuratively and literally; first in the Phædrus,[5] by the striking parable of the charioteer "Reason" driving a pair of horses, white and black, representing the higher and lower passions, then, at greater length, in the Republic,[6] where he compares the three kinds of soul with a small man, a larger lion, and a huge many-headed monster, joined together, corresponding respectively both to reason, passion, and appetite, and to the rulers, guardians, and craftsmen of his republic. But the most direct account is in the Timæus,[7] where Plato says that God, having created the soul of the universe and of the inferior deities, committed to these latter the formation of man. They, having received from Him the immortal principle of the soul, placed it in the head, and themselves constructed a soul of another nature which is mortal, placing it in the body cavity, the neck forming a sort of isthmus to save the divine as far as possible from pollution. Then they divided this mortal soul into two, using the diaphragm as a partition, like that between men's and women's apartments, the manly and passionate kind being above and the appetitive below.

[3] 5.429. [4] 5.309–431. [5] 246. [6] 588, see also 441. [7] 69.70.

This trinitarian doctrine has had a long history, and has sometimes been disputed with almost Athanasian vigour. Galen, in his commentary on the Timæus, complains bitterly of the abuse poured upon him by the Unitarians.[8] The point of controversy is, did Plato divide the "substance" (*οὐσία*)? Galen says he did, and does not hesitate to make him speak of "three souls" and "three substances."[9] In our text the philosopher is apparently careful to avoid the plural, but it seems a legitimate inference from the Timæus quotation that he maintained the existence of at least two souls diverse both in origin and faith.

The importance of the question is its bearing on that of human immortality. Is the whole soul immortal, or only its purely rational part? The former is the doctrine usually attributed to Plato, and Galen tells us that many of his followers held that "mortal" in the above passage is not to be taken literally, but means only that the soul in her lower aspects deals with transitory phenomena while pure reason surveys everything under the form of eternity.[10]

But, for Galen, it is this popular view which is not to be taken literally, being mixed with that noble or useful "lie" which the philosopher maintains may sometimes be told by the wise for the benefit of the vulgar.[11] Plato's true esoteric teaching is to be found in the Timæus, which was addressed originally to "a very few hearers."[12] The Pythagorean metempsychosis, too, is not to be taken seriously even in the Timæus. Plato there tells us that the secondary gods produced the nails in a rudimentary form in men (the first human beings created) since they knew that those who lived unworthily would degenerate into "women and the other animals" in whom the true use of nails and claws is clearly demonstrated.[13] This certainly seems not quite serious, and Galen characterises it as a "feeble" explanation.[14]

"Concerning the kinds of soul that are in the heart and liver, he [Plato] and I are agreed that they perish at death." "As to the rational part of the soul, Plato is obviously convinced that it is immortal, but I have no conclusive argument to advance either that it is or is not."[15] But he clearly considers that the balance of evidence is negative. The intellect seems almost as closely connected

[8] In Plat. Tim: § 20. [9] 10.635. [10] 5.794. [11] Rep: 2.389. Laws 2.663.
[12] 4.758. [13] 76. [14] 3.16. [15] 4.773, see also 4.701–702.

with the brain as are the passions with the heart. They undergo concomitant variations (συμμεταβάλλεται)[16] indicating that each kind of soul is something "of the body," probably its κρᾶσις or "temper." We recognise the well-tempered or well-blended man (εὔκρᾶτος ἄνθρωπος) by the excellencies of his mind even before we discover that he has also an excellent appetite and digestion.[17] The soul, reason included, is readily affected by wine, fevers, and poisons. It may be driven out of the body (on the Platonic theory) by a blow on the head, a draught of hemlock, or a great loss of blood. "If Plato were alive," says Galen, "I should like to ask him why this occurs, but he is absent, and his representatives do not explain it satisfactorily."[18] Their doctrine that the soul is immaterial, but uses the brain, etc., as its instruments, the phenomena above mentioned being due to variations and defects in them, but not in the soul itself, fails to satisfy him. He tells us, almost pathetically, that he has strained his intellectual powers to no purpose in the attempt to conceive immaterial substances or essences differing from one another and capable of such extension in space as to pervade the body.[19] Some Platonists might have said that he need not trouble about differences, which they attributed as he did to the varying "temperaments" of the body, by which the brain, "like a dome of many-coloured glass, stains the white radiance" of that pure reason which lives in the eternal. To which Galen, supported by Aristotle on one side and the common man on the other, might have answered, that it is just these colours, this individual diversity and personal temperament which seem to give most of its value and reality to continued existence.

Perhaps he said something of the kind in his lost commentary on the Philebus,[20] a dialogue in which Plato, anxious to prove that pleasure is not the highest good, attempts to consider separately a life of pure emotion and one of pure intellect. The young Protarchus is asked to imagine a being such as an oyster, capable of pleasure but devoid of mind. Suppose such pure pleasure, joy, ecstasy as intense and prolonged as you like, would you chose it? The youth says no, but rejects with even more emphasis a life of pure reason.[21] This is less clearly defined, but may perhaps be compared to a cherubic head, eyeless and earless (for, according to

[16] 4.782. [17] 1.576. [18] 4.775. [19] 4.776. [20] 19.46. [21] Philebus, 21.

Plato, "he who attains pure knowledge has got rid as far as he can of eyes, ears and the whole body")[22] engaged in the internal contemplation of mathematical truth as represented in those spheres and circles which Plato usually employs to express reason.[23]

Galen's remarks on the Philebus are lost, but his views on the most material aspect of the question are still extant. He knew the Christians, being, according to Harnack, the first pagan to mention them with respect; though he remarks that, as with the disciples of Moses, their principles are based on inadequate evidence.[24] He had doubtless heard of their strange doctrine of a "resurrection of the flesh" and an immortal body, and may refer to it in a passage from his commentary on Plato's Republic preserved by Abulfeda.[25] "Many men are unable to follow in their minds a consecutive argument. Hence they have to be instructed by parables, such as stories of rewards and punishments to be expected in a future life. Thus we see, in our time, that the people called Christians have derived their faith from parables." Apparently he considered that these parables, like those of Plato, were not evidence.

But his most definite remarks on the subject are connected with a curious episode of his own time. In the latter part of the second century there might have been seen in the streets of Rome an aged philosopher, whose venerable and decrepit appearance excited ridicule rather than respect. For, about forty years earlier, he had published a treatise in which he declared he had discovered a way of preserving perpetual youth. He was now about eighty years old and looked it; yet he had brought out a new and revised edition of his pamphlet "On Wonderful Agelessness," explaining that the treatment must be begun in early childhood, so that, since it was discovered by himself, he had been naturally unable to profit by it. But if anyone would trust his young children to him he would make their bodies immortal. Whereupon some did so, but the philosopher died, and his method perished with him before it had had a fair chance.[26] This man, says Galen, acted like the sophists who delight in paradoxes, and his assertion is contrary to all experience; but to dismiss him, by alleging as a self-evident truth,

[22] Phædo, 66. [23] Philebus, 62. Timæus, 40–44. [24] 8.579.
[25] Historia Anteislamica, p. 109. [26] 7.670 f.

that whatever begins must have an end, is not scientific, though he had himself used this argument in an earlier treatise.[27]

Plato had seen and surmounted the difficulty long before. He admits that the rational soul is both created and compound; indeed, he pictures the supreme Deity mixing its ingredients in a bowl, in various proportions for various creatures.[28] It is, therefore, not eternal, nor of its nature immortal, for what begins may end, and what is compound may be dissolved. Yet the soul is immortal by the will, or rather by the nature of God, for what He has joined in perfect and happy union, as is the case with souls of the universe, of the stars and inferior gods, and that in the human brain, none but an evil god could or would put asunder.[29]

All this was discussed by Galen in his favourite work "On Demonstration" or Scientific Proof (*περὶ ἀποδείξεως*) in fifteen books, which has been twice lost, though one MS. is said to exist "in the castle of a nobleman in Wallachia."[30] But a long extract from the fourth book has been preserved by John Philoponus in his attack on the Neo-Platonic doctrine of the eternity of the universe. Galen there[31] says that, though it is a self-evident truth that what has no beginning is imperishable (*ἄφθαρτον*) since it is eternal already, the converse statement, that what begins must perish, is not self-evident, for it may acquire a "reconstructive" (*ἐπισκευαστή*) immortality. He then quotes Plato's assertion in the Timæus, that the rational soul, though created, is immortal, and adds a commentary upon two rather obscure passages in "The Statesman,"[32] in which Plato attributes a certain immortality to material bodies such as the universe. Galen suggests as illustration a city, such as Sparta, which, though originating in time and itself in flux, may be conceived to become "eternal" if provided with a never-ending succession of inhabitants. Though the extract ends here, he probably went on to apply the argument to the human body, for he refers to this treatise for a further discussion of the theoretical possibility of the "wonderful agelessness" of the old philosopher, and the body may evidently be conceived as having an immortality of perpetual repair.

The same book also contained Galen's most definite opinion

[27] 6.63. [28] Timæus 41. [29] Timæus 41.
[30] I, cxcvi. [31] Teubner, p. 600. [32] 269,273.

on the immortality of the soul, and the passage was quoted by Bishop Nemesius in his work "On the Nature of Man."[33] "As to the rational soul he (Galen) expresses himself doubtfully in these words" . . . but all our MSS., both Greek and Armenian, omit the passage, the authorities thinking, perhaps, that the bishop's refutation would be more satisfactory without it. His answer is to the effect that the soul is evidently distinct from the body, which it uses merely as an instrument; and that, on Galen's theory, all matter must possess some kind of soul, which is absurd. We may, perhaps, conclude that Galen, as he indicates elsewhere, held that even the rational soul is possibly an effect, collateral with our activities, of growth and organisation.

In his extant works Galen shows much greater interest in the physiology than in the metaphysics of the soul. He was really an Aristotelian, with a healthy appetite for the actual, as displayed in observation and experiment, opposed to the Platonic idea that we can best contemplate the highest truth by internal reflexion freed from all sense interference. He perhaps held, like the young Protarchus, that a life of pure reason would be hardly more worth having than that of an ecstatic oyster, neither of them being a real continuation of human existence, and he certainly considered that the possibility of other forms of immortality, though not to be entirely rejected, was outside the limits of profitable discussion.

[33] Antwerp, 1565, p. 37.

FRAGMENT OF A PERSIAN PRIMER OF THE INSTITUTES OF MEDICINE

By R. Ramsay Wright, M.A., LL.D.,

Formerly Professor of Biology and Vice-President, University of Toronto

OF the hitherto untranslated Persian manuscripts in the Bodleian Library dealing with medical subjects, No. 1617, the subject of the present account, recommended itself for a first essay in this direction by its modest dimensions. It is described as follows in the Catalogue:

"An anatomical and physiological treatise, chiefly containing an explanatory description of the seven species of umūr i tabī'ī, viz., arkān, mizāj, akhlāt, a'ẓa, ruḥ and quwat. The seventh is missing as this copy breaks off suddenly on folio 34. Folios 35–37 deal with other matters, especially the science of the pulse (nabẓ) and therefore on the fly-leaf the Hindustani title (examination of the pulse) is given to the whole treatise.

"Folios 37, lines 13–18, partly Nasta'liq, partly Shikasta; by different hands; 8.5″ x 5″."

The description is inaccurate in the following particulars:

(1) The seventh of the Umūr i tabī'ī (af'āl) is discussed in folio 13, and the remaining folios up to 34 deal with the following topics:

Health and disease	folio 13*b*
Classification of diseases	15*a*
Causes of disease	19*a*
Six necessaries of existence	19*b*
Symptoms of disease	27*b*
Examination of urine	29*b*
Examination of fæces	32*b*
Explanation of the pulse	33*a*

(2) Folios 35*b*–38*a* in shikasta, but the same hand, do not deal with the pulse, but chiefly with a description of the battle in which Prince Kāmbakhsh was mortally wounded in 1708. This furnishes

the only clue to the date of the manuscript. As to the authorship, the only internal indication is a reference to a larger work by the author entitled "'uyūnu 'lhaiyāt," which I have been unable to trace.

After the customary invocation the author plunges at once into the discussion of the "naturals," those things which are characteristic of man and the constituents of his body. They are seven in number:

(1) The four elements, by the combination of which everything in the world, whether animal—including the species man—vegetable, or mineral, is made. Each element has two properties, fire being warm and dry; air, warm and moist; water, cold and moist; and earth, cold and dry. When the Almighty created the elements He assigned them a relative position according to their specific gravity.

(2) The combination of the four elements which is characteristic of man is known as his constitution or temperament. If left to themselves each element would tend to assume its original position; there must, therefore, be one which, being in excess, is enabled to take control and hold the combination together. If the excess is just sufficient for this purpose the constitution is termed equal-tempered, but this does not mean that there is an equal proportion of the elements. On the other hand, should the excess be more than sufficient, the constitution shares the properties of the predominant element. There are thus five different kinds of constitution.

(3) As a result of the digestion of food, there are formed in the body certain humours. The food first assumes a form like barley-water, the "chyle" of the Greek physicians, and is then conveyed to the liver, where it is concocted into "chyme." The nature of the chyme is necessarily dependent on the proportion of the elements in the food, and therefore where fire is predominant, it is hot and dry and is known as bile, when earth is in excess as black bile, when water as phlegm, and when air as blood. These are the four humours. Blood is particularly appropriate to life, for life is characterized by sensation and movement, the former demanding moisture, the latter heat. It is situated in the veins, and when any constituent of an organ becomes deficient, it is replaced by the blood, which takes on the nature of the organ in question.

Each humour may assume two forms, natural and non-natural.

Natural bile, e.g., is situated in the gall-bladder, and whenever the necessity arises for washing out the intestines, some of it is poured out and carries away the effete matter. But if it gets into the stomach, it causes good food to be evacuated or to undergo fermentation. Natural phlegm (lymph) flows in the veins from behind forwards, and whenever blood is deficient for the nourishment of an organ, phlegm is converted into blood by natural heat. It also replaces blood in the nourishment of the brain and spinal cord, because these are adverse to blood, and require nourishment similar in colour and nature to themselves. Phlegm has a strong resemblance to two other secretions, the saliva, which is concocted in the mouth and resembles the boiled rice used in dressing linen, and mucus, the viscid material eliminated from the nose.

The four humours must be present in a certain proportion, otherwise the predominance of any one is a cause of disease and corruption. The Greek physicians have established that there must be enough blood to nourish the body, and that the proportional amount of phlegm is one-half of that of the blood, of bile a quarter of the amount of phlegm, and of black bile an eighth of the amount of bile.

(4) The constituent parts of the body may be either simple or compound; the former, like flesh and bones, are constructed of similar parts, while the latter—the hand, for example—has various different constituents. Some say the heart is the warmest organ, some the liver; the brain is the moistest organ and bone the driest. The author does not accept the statement that hair is the driest organ, for he regards it as an excretion formed in the fourth concoction.

In this connection he refers to the four concoctions and their excretions. Some reckon five concoctions and assert that the first takes place in the mouth, but this is unsupported, for the first concoction takes place in the stomach, and whatever is not digested is expelled as fæces.

The second concoction occurs in the liver, and the urine represents its excrement; the third in the veins, where nature arranges that whatever is suitable for the nourishment of the organs is selected from the blood, while what is unsuitable is eliminated as sweat or sebum. The fourth concoction takes place in the organs, where the selected material is transformed into the substance of

the organs; any excrementitious matter is rejected through the pores, or if very dense is retained and attached to the body in the form of hair, while any surplus matter not required for the nourishment of the organ is conveyed to the testes in the male and to the breasts in the female. The matter so separated from each organ of the male and female assumes the same form in the body of the child by the power of God.

(5) The fifth of the "Naturals" is Spirit, and philosophers explain it as a subtile substance originating from the blood in the heart, and carried by the arteries to all the body. Three kinds are recognised: vital, natural, and animal or psychical, seated respectively in the heart, liver, and brain. Life is dependent on the first, nutrition and the related functions on the second, and the reasoning powers and sensation and locomotion on the third. The opinion has been offered that there is only one kind of spirit, performing different functions according to the organ in which it is situated.

(6) The energies, faculties, or powers form the sixth category of the "Naturals." Like the spirits, they are vital, animal, and natural; life is primarily dependent on the first, sensation and movement on the second, and nutrition and growth (which are unconsciously exercised and are also present in plants) on the last.

Of these it is necessary to distinguish principal and subservient powers; the powers of nutrition which affect the whole body have as subservient powers attraction, retention, digestion, and expulsion. The powers of growth preside over growth conformably to the typical dimensions of the species, and include the power of procreation, in virtue of which the sperma genitale is prepared and separated from all the organs of the body, and the formative powers, so called because each particle of the sperma genitale assumes in the child the form of the organs of its father and mother from which it was separated.

The animal powers are concerned in movements, either for expression of the emotions or for locomotion and also in intellectual processes which deal with external and internal phenomena. Those dealing with external objects are the five faculties of vision, hearing, smell, taste, and touch. They are like spies which report to the internal faculties. Vision resides in the optic nerves, which are hollow and cross on their way to the eyes. Some assert that the crossing

is not complete, but by all accounts this spot is the site of the visual faculty. As to the method of vision there is some discussion: some say that rays of light proceed from the pupil and are reverberated to it from the object; others that an image is formed in the pupil just as in a mirror.

The sense of hearing is situated in the drum of the ear, which is nervous, and is affected by the impact of particles of air caused by sounds. The sense of smell is related to two bits of flesh resembling nipples inside the nose, which detect odorous substances, and that of taste to nerves in the tongue, which are stimulated by savoury substances dissolved in the water of the mouth. The skin is interwoven with the nerves of touch, which distinguish hardness and softness, heat and cold, moisture and dryness.

The intellectual faculties are also five in number, viz., the sensus communis, the imaginative faculty, the estimative faculty, the cogitative faculty, and memory. These are situated in different portions of the brain, which are lodged in different fossæ of the skull. In the skull there are three fossæ, the two foremost of which are divided into anterior and posterior compartments. In the anterior compartment of the foremost fossa, the sensus communis is lodged, and imagination in the posterior compartment. The estimative and cogitative faculties are situated in the anterior and posterior compartments of the middle fossa, while memory occupies the third fossa.

(7) The seventh category of the "Naturals" is that of the operations or functions. They may be simple or compound; swallowing is one example of the latter, involving as it does both attraction and repulsion. These operations, like retention, are brought about by muscles disposed longitudinally or transversely.

Health and Sickness. The physician must recognise that there are two conditions of the body, one in which all the functions are working naturally and another in which all or part are not in natural condition. Abu 'Ali, quoting from Galen, distinguishes in the Canon an intermediate condition, such as convalescence or infancy, in which health and sickness coexist, but their arguments are feeble, and have been refuted by the author in his treatise "'Uyūnu 'lḥayāt." Health is either complete or incomplete, and the illness of the individual should be referred to under the name of the organ

concerned. The blind man, e.g., may declare that there is nothing the matter with his health.

Classification of Diseases. Diseases may be subdivided into two groups, simple and compound, and each of these again into several subgroups. A simple disease is that which results from failure of health in regard to one function, and a compound one in regard to more than one.

Simple diseases may be classified according as they occur at first in a simple organ, or in a compound one, or in a simple and compound one at the same time. The first is referred to as badness of constitution, the second as mixed, and the third as solution of continuity. Diseases of constitution are of eight kinds, according as the departure from health is in respect of one of the elementary properties (heat, cold, etc.) or of two. An increase of bile, e.g., is characterized by heat and dryness.

The mixed diseases are of four kinds, viz., disease of form, of size, of number, and of position.

Solution of continuity may occur in the skin, resulting in an excoriation, or in the soft parts in an abscess or fistula, or in the bones in a simple or compound fracture. If it occurs in a vessel or nerve it is curable, but in the heart is fatal.

Compound diseases are those which result from the conjunction of several diseases. They are named in reference to position or size or to the organ most concerned or to some assigned cause. Thus pleurisy receives its name from the side, elephantiasis from the resemblance of the patient's leg to an elephant's, and melancholy from the black bile which causes it. Many names come from some symptom characteristic of the disease, such as epilepsy from falling, and apoplexy (sakta) from loss of speech.

Every disease occurs independently or is associated with another. The original disease may show itself first by a secondary symptom, e.g., the headache due to disease of the brain is accompanied by defects of vision, or the enlarged glands in the axilla which occur in a case of plague. Also an organ may become the receptacle of corrupt matter formed elsewhere, the axilla, e.g., from the region of the heart, the ear from the brain, and the groin from the liver. Should treatment applied to the secondary symptom show no result, then remedies must be directed to the original source.

The physician must pay attention to the four periods of a disease, viz., the onset, increase, decrease, and termination, so as to adopt his treatment conformably to the conditions of each. For example, should there be fever in a case of dropsy it would not be proper to prescribe cooling drinks, and should coughing occur along with diarrhœa it would not be advisable to treat the cough with mucilaginous drinks, which would increase the purging.

Several diseases are communicable from one person to another. (Here a couplet as a Memoria technica.) They are elephantiasis, scab, smallpox, measles, plague, leprosy, foul ulcer, and ophthalmia. The communication takes place the more rapidly when the wind blows from the direction of the patient.

There are also diseases which are transmissible by heredity from father and mother (another couplet), they are gout, consumption, white leprosy, piles, fœtid breath, epilepsy, black leprosy, ophthalmia, foul sores, measles, and melancholy.

Causes of Disease. Whether the body be healthy or sick, a cause for such condition is necessary, which may be external, internal, or antecedent. Such a cause may have a secondary action differing from its primary action. Thus scammony produces a warm complexion, but after it has expelled the bile from the body, cold results. A cause is either necessary or non-necessary; drinking poison, e.g., is a non-necessary internal cause opposed to nature.

The Six Necessaries of Existence. But there are a series of necessary causes without which life and health are impossible.

(1) The first of these is the atmosphere which surrounds the body, which if impure is a cause of sickness. There are certain natural alterations of the atmosphere proper to the different seasons which bring with them their characteristic diseases. Thus diseases of the bile are common in summer, of the phlegm in winter, of the blood in spring, and of the black bile in autumn. Alterations of the atmosphere may be due to celestial or terrestrial causes. An example of the former is the cooling of the air due to an eclipse of the sun in summer, or the additional warmth in winter due to approximation of a planet to the sun. As an instance of a terrestrial cause, the situation of a city on the western slope of a mountain may be cited. Here the sudden change of temperature when the sun reaches the zenith is a frequent cause of sickness, and besides the mountain

is an obstacle to the east wind, which is regarded by physicians as the same as the zephyr. In every city in which the atmosphere is very cold, the body is fortified, the digestion improved, and the complexion redder.

(2) Food and drinking constitute the second of the six necessaries of existence. It is necessary to study the effect of substances introduced into the body. They may act either in virtue of the food-material they contain, or of certain properties or certain specific peculiarities. Lentils and barley gruel may be taken as an instance of the first, pomegranate and lettuce of the second, while the specifics may either have good properties, as theriaca, or bad ones, as poisons. One substance, however, like wine, may act in all three ways.

Some foods yield dense, others thin blood, and others again well-proportioned blood. Beef and bread and butter are an example of the first, chicken of the second, and one-year-old lamb or veal of six months of the third. Again some, like soft-boiled eggs, are entirely converted into blood; some, like leavened bread, only partially, and others, like duck and old beef, not at all. There are combinations, like fish and sour curds, which should not be eaten together, and foods which are gross or high should be avoided. Even although no ill-effects should be experienced, they are harmful in the end. A man who has fallen off his roof without breaking a limb should not on that account refrain from the use of the ladder.

Whoever persists in the custom of drinking milk is eventually seized with palsy or other chronic affection like leprosy. The number of meals should be such as to allow of the complete digestion of the food before more is taken into the stomach, and too many different kinds of food should not be taken at the same time on account of their variable digestibility. Foods should be suited to the temperament; a person of sanguine complexion, for example, should avoid fat and sweet things, especially honey and dates.

As to drink, only so much water should be taken as will make up for the dryness of the food, and then one hour after eating. A little before eating is permissible in the case of those persons of bilious complexion who have no desire for food till they have first drunk water. Similarly drinking water fasting is forbidden except in the case of a person who has drunk wine overnight, and whose

liver in consequence is inflamed; but gradually the evil effects of such water drinking appear in the body, and this is one of the disadvantages of drinking wine.

As to wine-drinking the author will speak with no uncertain sound, because in addition to being prohibited, it brings with it such pernicious effects both in this world and the next. Even a moderate indulgence is bad, because although the appetite may be improved and the body strengthened, yet eventually the dose has to be increased till it becomes excessive. Sometimes the drinker will abstain for a time in the hope of finding some text in the sacred Qu'ran permitting the manufacture of wine from grapes, but the Prophet has said in the passage on wine and gaming, "the Sin is greater than the profit." There are, however, advantages to man in the use of wine as a medicine, provided it is administered by an intelligent physician, but spirits extracted from molasses, dates, and the like are wholly deleterious.

A further recommendation as to water-drinking is "the less the better," for the Prince of Physicians, Hippocrates, says, "whoever desires a long life should drink little water, eat his food in the morning, and keep away from women."

(3) Movement and rest have each advantages; the former favouring peristalsis, the latter digestion. Movement must not be too violent, but rather moderate, such as walking about a garden or playing with a gazelle or gentle exercise on an easy-going horse, but if there is great oppression, then harder exercise on foot or on horseback may be advantageous. Rest should come after meals, and one hour is prescribed in Hindostan for this purpose.

(4) But there are also psychical movement and rest, and there should be a proper equilibrium between them. Too much emotion, whether pleasurable or the reverse, may be dangerous, because of the sudden movement of the spirits outwards and inwards; but too little produces apathy and stupidity.

(5) Sleeping and waking are also necessaries. In the latter state the external and internal senses are entirely in a functional condition, similarly the limbs are often in motion, so that after a time sleep is necessary to remove the fatigue of the senses and limbs. Both must come into play moderately, for insomnia is the cause of dryness of the brain and melancholic diseases, while too much sleep

produces phlegmatic diseases. When the stomach is empty, sleep is not good, and indeed the digestion of heavy food is favoured by sleep.

The best time for sleep is the first part of the night. Sleep during the day is not good, especially in winter; if it has become a custom in summer it should be discontinued by degrees, but if there has been great physical or mental exertion a short time during the day should be had for the repair of fatigue, but more than one hour is not permissible.

(6) Evacuation and retention constitute the sixth necessary of existence. If the excreta are not removed from the body, illness and death result; the same is true if the healthy humours are not retained within the body. Excessive evacuation is the cause of dryness, coldness, and leanness of the body, and excessive retention of obstruction, oppression and loss of desire for food.

Whoever carries into effect the foregoing recommendation with regard to the six necessaries of existence will require neither medicine nor a physician. Should anyone wish to argue that they should have been reckoned as eleven, the answer is that those that are in twos are counted as one, both being opposite and never coexistent.

The Explanation of Symptoms. According to physicians symptoms fall into two categories, (*a*) those which are indicative of the natural temperament of the patient, (*b*) those indicating something accidental to his temperament. For the purpose of systematization ten kinds of the former are recognized: (1) Surface temperature. (2) Condition of muscular system and amount of fat. (3) Character of hair. (4) Colour; if pale, it is a sign of a cold and moist constitution; if red, of one hot and moist; if yellow, hot and dry, and if dark, cold and dry. It is difficult to form any conclusion from the complexion of a negro. (5) Development of the chest. (6) Actions, such as gait, conversation. (7) Impressionability. (8) Sleeping and waking. (9) The excreta. (10) The psychical functions.

The excess of any of the humours may be distinguished by various signs—by bad dreams, for instance. If the patient dreams of bright lights and fire, this is a sign of the excess of bile; if of carrying heavy burdens, an excess of blood; if of waters and seas and clouds, an excess of phlegm, and if of black things like elephants and smoke, an excess of black bile.

The physician must also give precedent consideration to the climate in which the patient resides, whetherit be the stimulating atmosphere of Kashmir or the close atmosphere of a city of the plains.

Examination of the Urine. The characteristics of the urine to which attention must be given are seven in number: (1) Colour, (2) density, (3) clearness or turbidity, (4) smell, (5) froth, (6) deposit, (7) quantity.

The young physician is warned that he may be led into terrible blunders if he is unfamiliar with the effect on the colour of the urine produced by the patient having coloured his feet with henna in the evening; it becomes green to red and afterwards very dense. So also he must be able to distinguish pus from other deposits.

Examination of the Fæces. Here also the colour, consistence, smell, and quantity form valuable guides to the physician.

Explanation of the Pulse. Since the throbbing of the artery at the wrist is a guide to the nature of a patient's constitution, the various symptoms have been studied and established. The indications derivable from the pulse are dependent on the fact that the arteries grow out from the heart, as the caval veins do from the liver, and as the function of the latter is to cause food to arrive at the organ, so that of the former is to bring air to the heart for the sake of rectifying the spirits and ejecting the warm and effete breath. Moreover, the perpetual motion of the arteries is necessary for seizing the air, and their dilatation is required to ensure its penetration by means of the tubes, and their contraction to expel the heated air.

This whole question is deserving of minute consideration, on which account it is treated in detail in the author's larger work 'Ugūnu 'lhayāt. Since, however, this abridged brochure has been prepared for the requirements of the physician, and the knowledge of all the niceties is not necessary for him, the author restricts his pen from enlarging on this topic, retaining only what is necessary for the cure of disease and the preservation of health.

These are the different characteristics of the pulse which must be examined: (1) Dimension, (2) strength, (3) celerity, (4) resistance to pressure, (5) period of repose between beats, (6) temperature, (7) fulness or the reverse, (8) uniformity, (9) if equal, either ordinate or inordinate, (10) rhythm.

Special names have been given to various combinations of these

characteristics, in order for purposes of diagnosis to obviate detailed description. Such are the expressions: (1) Serrate, (2) undose, (3) vermicular, (4) formicant.

The MS. breaks off in the definition of the last mentioned of these characteristic varieties. It will be observed that the author has adhered very closely in the arrangement of his material, and indeed sometimes to the text of the 1st and 2d sections of the 1st Book of the Canon of Avicenna. The scope of his Primer was evidently intended to be similar to that of the Isagoge of Joannitius.

THE INNATE HEAT

By Professor Sir T. Clifford Allbutt,
Regius Professor of Physic in the University of Cambridge

WHOSOEVER may have watched a bee buzzing against a windowpane, and then, as it finds an open casement, darting out of sight on wings whose vibration is so rapid as to be invisible, such a thoughtful observer may often have wondered whence comes this marvellous power of motion in living things? And so wondered the wise men of Ionia, twenty-five centuries ago. The philosopher who throws a stone sees motion communicated from his living hand to the dead matter; but even in the sixth century B.C. the philosopher did not stop there. He had extricated his thought from crude animism, and perceived that motion was not peculiar to living things and their effects. He saw, for example, the vapour arising from the sacrifices of the temples (*anathumiasis*) yet, as this arose from things lately alive, it might be an exhalation, a departure, of the lively spirit of them. Still, as he looked again, he saw vapours arising also from waters; moreover, the celestial bodies were in motion, and as his eyes were bent to his own hearth he saw the sparkle and leap of fire, the most nimble of all things—even more nimble than any animal. The hearth fire seemed to be animated by a quality of levity, the contrary of heaviness; and the swift coursers of heaven themselves seemed to be fiery. Was not fire, then, the source or agent of motion, fire and the heat of it in all things? And thence the ancient thinker made another stop in his thought; as he watched the smith or the potter he saw that fire was of two kinds, destructive and constructive, a destroyer but also a maker; and under these conditions demiurgic.

"Καῖ νὺν φλόγωπον πῦρ ἔχουσ' ἐφήμεροι
"ἀφ' ὄυ γε πολλὰς ἐκμαθήσονται τέχνας.

"In the fiery flame that lends
Its aid to every art."

Again, the Ionian philosopher could not think long of fire without thinking also of air, the close ally of fire if not indeed of the same nature. That air was a material substance was not evident at first to these sages. Zeus, the æther of the celestial spaces, in which coursed the sun and other fiery bodies instinct with heat and motion, an æther highly rarefied but yet subject to condensation into functions of matter, seemed to be the sphere of most intense motion, molar and molecular. So the Ionian philosopher divined that heat consisted in an intense inward expansive molecular motion, a concept afterwards forgotten until revived by Francis Bacon in the classical passage of the Novum Organon (Fowler's Ed. N.O. pp. 368–70). Moreover, in representing the thought of Ionian times, we shall not forget that, by the genius of Leucippus and Democritus, evolution was founded upon an atomic hypothesis; and not only so, but also on the boldest intellectual lines of the indestructibility of matter and force; on expansions and condensations, attractions and repulsions of the atoms of a primordial stuff; and this in a cosmos of number and law. Thus Empedocles, Anaximenes, Diogenes of Apollonia, Heraclitus, taught that fire was the finest and subtlest air, such as was around the sun; and, still more definitely, that there was a something creative between air and fire, a demiurgic essence, a dynamic stuff, a spirit of motion and heat—to use Bacon's words, "The spirits of animals and vegetables are compounded of an aery and flamy pneumatic body." This subtle principle, broadly speaking, we may identify, or compare, with the fifth essence—the quintessence—of Aristotle, which seemed to Harvey the only possible source of perennial energy, such as that at which he marvelled in the heart.

Let us turn now from the macrocosm to the microcosm; and in particular to that mysterious mechanism the respiration, a function which has fascinated mankind from time immemorial; from the time when the spirit of God moved upon the face of the waters, and God breathed into man the breath of life—the *beseelte Luft.* Indeed as to-day we utter the word "inspiration" we feel the glow of the spirit which, from those ancient legends of the creation of life to the messages of our modern ethereal telegraphy, from the hauntings of the Great Spirit in primeval man, through the storms of superstition, to the haven of the soul in its purest communion

with the Divine, has moulded the whole story of man and embedded itself in his tongue. Something ethereal in the breath of life, something living in the rhythms of the heavens, Galen's "fiery and intelligent divine activity," we may follow onward through the centuries as the *impetus faciens*, *causa efficiens*, *aura genialis*, *spiritus seminis*, *spiritus rector*, *mysticum spiramen*, phlogiston, caloric, vitalism, and so forth. What, then, is this elusive but all-pervading, this mysterious yet all familiar, this universal yet directly personal influence which we can neither seize nor escape from; what is its secret, where is the abode of it?

If inspiration is just air, what of air, or in it, can be fraught with creative power? What airy agent can endow the tabernacle of clay with energy, life, motion, and thought? Is it that in expiration the soul goes out to make touch with the universe and to return with a *spermaticos logos*, able to engender things and knowledge? In our own time Laurence Oliphant wrote: "The sense of union with Christ, or His living in us, is manifested, or becomes perceptible, in a physical sense, chiefly in the natural respiration." Professor Mott, the other day, told the Society of English Singers that the emotions established a continuity and meeting place of psychical and physical forces in the breath. And by many of the ancients the breath was recognised not as a function of the lungs only, but of the skin also; indeed, of the structure of the whole body which was pervious to air and fire; a vortex of the *respiratio mundi* of the macrocosm; a fiery air animating both the animal and the universe, and appearing as motion and life. As with the insight of genius said Heraclitus, "this animating fire (πῦρ αἰείζωον) was not visible flame; it was something subtler, something *between* air and fire, penetrating and vitalising everything."

The Pre-Aristotelians, for the most part, regarded respiration (let us confine ourselves to the warm-blooded animals) as the chief path by which this subtle fiery air entered and penetrated the body. But meanwhile another stream of thought, another interpretation, was gathering volume, and gaining an ascendancy over current opinion, especially in the Peripatetic schools. Diocles of Athens—an illustrious physician of the first half of the fourth century, upon whom was bestowed the great name of the Second Hippocrates, who was, moreover, the author of the first book of anatomy known in

history and of the first book on pharmacy—Diocles, under the influence of the Italio-Sicilian school, maintained and taught a doctrine very different from that of the Ionian schools which hitherto has occupied our attention. The observation of Diocles was fixed less upon the æther—the substance between air and fire—and the respiration, more upon the processes of digestion. He likened digestion to a fermentative process; and, not without reason, saw in the digestion and abdominal viscera a reservoir, and indeed a source, of animal heat. As an anatomist he had distinguished the lower vena cava from the aorta; he regarded the liver as the factory wherein blood was made from food, and supposed that the heat thus generated, but also otherwise reinforced, was carried to the heart which was the heat centre of the animal system. It was in the doctrine of Diocles that the hegemony of the heart, afterwards a central feature of Aristotle's physiology—in contrast with the truer idea of hegemony of the brain held by that mighty shade of ancient medicine, Alcmæon—found its first explicit form.

I have said "with some reinforcement otherwise." The terms psyche and pneuma were used by the ancient Greek physiologists without strict definition; even Aristotle was inconsistent in the use of them; consequently we cannot as historians always use and compare their opinions on these subjects with accuracy. It is not clear how far Diocles, and before him Empedocles, apprehended a physical begetting of heat in pepsis and "coction"; certainly they supposed some farther source to be necessary, a vital energy which was said to enter by this way or that according to the various opinions of teachers and sects. The point of interest is that while some teachers, such as Diocles, seem to have supposed the animal heat in some measure at any rate to be engendered in pepsis, others believed that this active essence came in wholly from without; others indeed, such as Aristotle, said that digestion presupposed this essential energy, as the natural and primary source of heat (*ἀρχὴ θερμοῦ φυσική*). This and such hypotheses hardened into the Aristotelian dogma of *ἔμφυτον θερμὸν*—Innate Heat, a dogma which governed physiology down to the day of Thomas Willis. From the fiery something in the air acting by way of the respiration, something which, as the earlier observers perceived, penetrated the whole body and altered the colour of the blood; or again from the half thought out

notion of Diocles that animal heat was engendered in pepsis and coction (fermentation), we find Aristotelian physiology pinned down to the notion of an uncaused entity—innate heat, radically distinguished from ordinary heat, akin to the "quintessence," and seated, as this school supposed, in the heart; or, as Harvey, and Empedocles before him, supposed, in the blood.

How, then, did this uncaused entity, Aristotle's nourishing, growing, and generating soul, get into the system? To this question the great Master, and his successor Theophrastus, gave little heed; they took it to be an implanted quality inherited once for all, both as to *quale* and *quantum*. Others, as we gather from the Timæus of Plato and other sources, supposed the *zoon* to be already *plasthen* when this dynamic essence was added to it; and they still kept the idea of the whole body being pervious to air and fire. Straton of the same school held that the spirit was carried in the semen. Thus the idea of combustion was lost,[1] and the part of the respiration was degraded to that of mere cooling of the innate heat. Neither Aristotle nor Harvey perceived the need of the tissues for air; hence Harvey's wonder why the blood should have to run round the body so many times a minute.

The Hippocratean tradition had been petrifying into Dogmatism; yet, speaking generally, it had retained the idea of the respiration as feeding the heat of the body; but the later Hippocrateans began to vacillate, and when in the Corpus we come to the Cnidian treatise on the Heart (*π. καρδιής*), a treatise of Aristotelian age, we find heat as an entity lodged in the heart, and thence distributed to the body; when in excess it caused fever. This anonymous author carried forward to Alexandria the doctrine of innate heat, and the notion of respiration merely as a cooling process (see Ritter and Preller, p. 113). However, in Alexandria, Herophilus and Erasistratus (*c.* 300 B.C.), so far as we can judge from the few relics of their works, at any rate Erasistratus, broke through the doctrine of the congenital heat or pneuma to some extent, and regarded the arteries (which in their dissections they found empty of blood) as the channels of the pneuma. Erasistratus still held that the animal heat, or pneuma, was drawn from the air, and carried by the lungs

[1] Aristotle used *πνεῦμα ἔμφυτον* and *φυσικὸν πῦρ* in the same sense (See Parv. Nat. 475*a* and 474*b*).

to the heart; thence the animal soul was delivered to the body and the physical soul to the brain.[2]

In Rome, Athenæus (about middle of first century A.D.) and the Pneumatist Sect for the most part followed Aristotle in the doctrine of the Innate Heat, the cooling function of the lungs, and the hegemony of the heart. But they amended the doctrine in this way, that they did not accept the innate heat as uncaused; after Diocles they supposed it, in part at any rate, to be generated in digestion.

Galen's view of this problem (later second century A.D.) is not quite easy to discern and represent. Huxley, in his Harvey Lecture, Nov. 2, 1878,[3] spoke as follows:

> "Part of the blood, it is supposed, went through what we now call the pulmonary arteries, and branching out there, gave exit to certain fuliginous products, and at the same time took in from the air a something which Galen calls the pneuma. He does not know anything about what we call oxygen; but it is astonishing how easy it would be to turn his language into the equivalent of modern chemical theory. The old philosopher had so just a suspicion of the real state of affairs that you could make use of his language in many cases if you substituted the word oxygen for the word pneuma."

This is true; but Huxley had not pushed his study of Greek physiology beyond Galen, or he would have seen that the "something between air and fire" had been apprehended far more clearly six or seven centuries before by the Ionian Greeks; and that Galen, under the influence of Aristotle, had somewhat muddled the clearer insight of his earlier forerunners. Unfortunately he adopted also the Peripatetic doctrine of Innate Heat and the function of the respiration as a cooling process; thus in his confusion doing justice to neither thesis. This unfruitful Aristotelian tradition he passed on through the wilderness of the Middle Ages and later, down, let us say, to the time of Leonardo, who again distinguished the scarlet from the venous or dark blood, and showed more precisely that it was the air which brought about the change. Cæsalpinus (sixteenth century) taught that a *spiritus* mingled with the blood in the arteries, and *moved* the blood. Harvey, who, not unnaturally, as things then were,

[2] For Erasistratus the souls were two, not three: see also Hipp. De Victu.

[3] "Lectures and Essays," p. 441.

detested the chemists, and so the chemistry, of his time, relied, as we have seen, on the Innate Heat, and on the derivation of the motion of the heart from the celestial essence; so he likewise regarded the lungs as cooling fans.

It was Willis (1621–1675), a few years younger than Harvey, who made the decisive return to biochemistry; he, and his pupil Lower after him, experimentally demonstrated the reddening of the blood by the respiration, admitting and excluding the air. In the second and fourth chapters of his Second Book ("Op. Omn. Vene.," 1708) Willis says that the animal spirit is not only a substance in space, but also by nature a certain kind of fire or flame, or a vapour or breath of flame (*halitus*, or *substantia flammæ*), or something akin to this; and that the spirit in the blood makes some kind of combustion (*accensio*), though not visible as shining or sparkling. Wherever there is animal life there is fire of a nitrous or sulphurous nature, and this is quenched at once if air be withdrawn. Now, on the other hand, if we turn a century backward—say to Fernelius—we find the Galenic muddle of respiratory theory between cooling and combustion still surviving; though Fernelius does admit that if air be withdrawn the animal does not die for lack of cooling, but by suppression of the fumes *insiti caloris*. John Mayow of All Souls (1645–1679), almost adopting the very words of the great Ionians, found in the air, and in saltpetre, a *spiritus nitro-aerius*, a *particula igneoaeria*, which consisted in a swift movement of contiguous particles or subtle atoms, dependent upon a sulphurous or nitrous element derived from the ambient air. Mayow writes: "Breathing brings the air into contact with the blood to which it gives up its nitro-aerian constituent. Again the motion (of the muscles) results from the chemical reaction in the muscle with the combustible matter contained therein." Then Boyle (1627–1691) on small animals, and on candles, in his air pump demonstrated the *pabulum ignis*. Thus, still in a crude way, these ardent searchers got still nearer to the discovery of oxygen, a discovery, however, to be deferred for another century. Priestly and Lavoisier brought the long and pathetic search for oxygen to its triumphant achievement in 1771.

ON THE SIZES OF THINGS, OR THE IMPORTANCE OF BEING RATHER SMALL

By A. E. Boycott, Radlett, Eng.

Creavit in cœlum angelos, in terram vermiculos: nec maior in illis nec minor in istis

If Augustine had gone, as any good bishop might go nowadays, to the natural history museum in the Cromwell Road, he would have found the text for many a useful sermon in the central court: how easily the seeds of sin may creep unheeded into army biscuit and how really terrible the devil is when you get a good look at him in a waxy trypanosome; he would have laid in a stock of pamphlets for unobtrusive distribution among his friends at home who were liable to Manichæan error, and he would certainly have noted the horrid deceitfulness which may be practised by innocent-looking butterflies. But not the least of his interest would have been touched when he came towards the stairs which lead to that sad refreshment room and found an elephant and a mouse mounted together upon the same board. "Nec maior in belua nec minor in musculo" might have been his meditation 1500 years ago: which we translate to-day into a reminiscence of "fiddling work making fleas" and go up the steps.

Beyond the facts that, on our human scale of values, the elephant is very large and the mouse is very small, I do not altogether understand what educative purpose the exhibit professes. It gives one indeed a comfortable feeling of respectable mediocrity; the elephant, it is true, is very much larger than we are, but he is extravagantly conspicuous and after all is very stupid, while as for the mouse—well, it is really rather amusing that such a wee thing should be. Except for something of this sort it is not very easy to see what meditations are likely to arise from contemplation of the sheer dimensions of the animals more satisfactory than those engendered of a six-legged calf or other miracle. But if one reflects briefly on the circumstances which attend greatness and smallness in animals, on the consequences, and if we may on the causes, of differences in

size, if in short we consider the beasts as live animals rather than museum curiosities, we come to a series of questions which seems to ramify in most directions. Some of these I will shortly state.

The thesis is that absolute size is worth consideration in biology. And it must be premised that the data necessary for its complete defence are not very easy to come by. For the last hundred years zoology and botany have been in the main occupied with considerations of an anatomy which is essentially comparative, and that *Lepus* is larger than *Lumbicus* has been a good deal overshadowed by the fact that each has nephridia and a cœlom. Attention has chiefly been bent on relative rather than absolute phenomena—using a phrase which, meaningless enough in the last resort, has quite a clear intention. It may be a happy world which thinks of similarities rather than differences, but as a consequence we still await the biological calendar of which Stephen Hales was dreaming nearly 200 years ago: "The most likely way," wrote the ingenious minister of Teddington, "to get any insight into the nature of those parts of the creation which come within our observation must in all reason be to number, weigh and measure." He was in truth before his time, though it is by one of its curious vagaries that the human mind has so successfully applied his method to dead things and as resolutely excluded it from the real world which moves upon that measured background. The fundamental truths of variability and adaptation do not make the size of an animal any less a definite fact of nature than is the supposed atomic weight of an alleged element.

Why is there no mammal larger than an elephant[1] and none smaller than a shrew-mouse? It is easy to say, and not very difficult to believe, that mechanical difficulties of support and progression are of moment in fixing the upward limit, while considerations of relative surface, body temperature, and possible rates of metabolism have determined the lower point. A good big elephant weighs five tons; a whale that does not need to walk may be fifteen times as heavy. A mouse of 20 grammes weighs 1/250,000 of the elephant, but his surface is about 1/4000 as great: a mammal the size of a house-fly (and there is plainly no difficulty in including all the anatomical

[1] For our present purpose we may agree with Moses and Mr. Gladstone that whales are fishes.

complexities of a mammal within such dimensions) would have to burn at a desperate rate to keep up his body temperature on a cold day; the elephant can let a mouse-thickness of his surface fall to any temperature without being much the worse.

But, as Augustine would surely have reminded us, the same phenomenon is reproduced in animals other than mammals and birds. About the biggest fish is a shark (*Selache*), which is described as 40 feet long and of a placid disposition; the smallest a mite (*Mistichthys*) of half an inch. The largest English butterfly is, I suppose, *machaon* (which is not so very big), the least *Lycæna alsus* (which is not so very small). *Nanosella*, $\frac{1}{4}$ mm. long, is said to be the smallest known beetle; the tiniest dragonfly is about $\frac{2}{3}$ inch across, the largest (and that of carboniferous times) about a couple of feet. There are indeed no insects which may be called big from an anthropocentric point of view, nor any which are invisible to a skilful myope. The same is true of snails: *Carychium minimum* is quite easy to see, and of the giant *Bulimus* a man could carry home a good many.

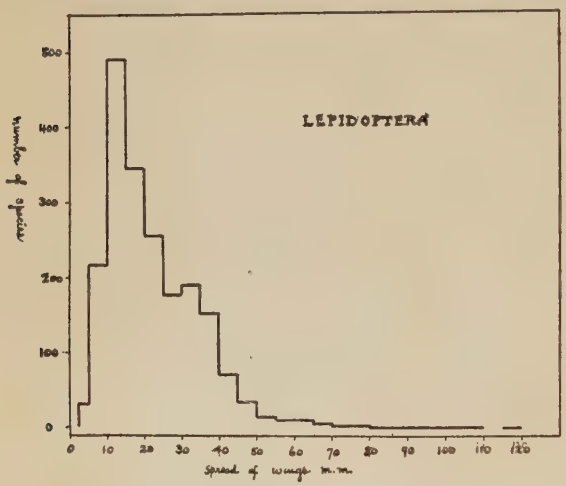

FIG. 1.

The data available for a detailed examination of this question are, as I have mentioned, rather meagre. Taking what is easily got, an analysis of the body lengths of the 3453 British beetles for which measurements are given by Fowler and of the spreads of the wings in the 2055 lepidoptera described by Meyrick yields the entertaining results shown in these two graphs. The mean length of the beetles is 4.6 mm., the smallest $\frac{1}{2}$ mm. (*Enconnus nanus* and *Hypocyptus punctum*), the largest 42 mm. (*Hydrophilus piceus*). But the largest length group is 2–2.9 mm., which contains 24 per cent of the species,

and 70 per cent are under 5 mm., 92 per cent under 10 mm. and only 1 per cent over 20 mm. Similarly the moths and butterflies range from 3½ (*Nepticula microtheriella*) to 117 mm. (*Acherontia atropos*) with a mean of 22 mm.; 66 per cent are less than 25 mm., 97 per cent less than 50 mm.

These figures lead to the same conclusion. The size of beetle or moth which fits in best with the rest of the world is quite small, and not very much above the lower limit of size found for its series. Spreading away far above this modal point are a diminishing number of scattered large species. Below it is a more compact group, but a group which is not numerous—only 3 per cent of the coleoptera are less than 1 mm. long and less than 2 per cent of the moths are under 5 mm. For mammals, fishes, and the rest, I have no quantitative data, but it may pretty safely be assumed that the distribution of sizes among them follows the same plan.

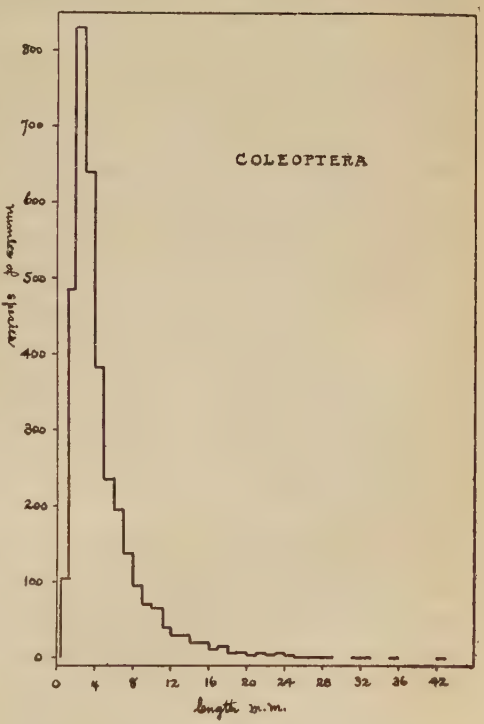

FIG. 2.

The difficulty of large animals is thought in a general way to be one of feeding a number of approximate spheres on a flat surface. The lower limits of size are presumed to be determined by the difficulty of compressing a complex structure into a small space, though if this is really so one would expect to find more evidence of simplification of structure as one approaches the minimal size. There are of course a great number of small ways in which increase of size and increase in complexity go together. But the differences are not dramatic, and the range of complexity, if we measure it

aright, is much less than the range of size. The preformationists found respectable citizens in the heads of spermatozoa, and Dr. Sharp says that the smallest beetles have as much anatomical complexity as the largest insects. Whether this is incompatible with the general zoological doctrine that increase in size is accompanied by increasing anatomical complexity and specialisation is a question of degree rather than of kind: it depends on the point of view.

While there is something incompatible with being a snail or a beetle or a mammal and being less than a certain size, living organisms as a whole know no such limits. Bacteria and protozoa form groups which show the ordinary facts about their upper limits of size; downwards they pass by insensible gradations to dimensions where, if we can see that they are there, we can form no just appreciation of their size and shape. The smaller visible bacteria are in a region of size where surface becomes a dominating factor: one wonders what sort of cellular architecture maintains Pfeiffer's organism in a bacillary shape. Beyond this we come within the range of molecular dimensions and begin to wonder again whether properties and substances are as discrete or as conjoint as we thought they were: "natura in minimis maxime miranda," said Linnæus.

Taking then a survey of the whole animal series, or of any group within it, we cannot well escape the conclusion that small sorts are more advantageously placed than their larger relations to meet the rough and tumble of life. What are the relations to the troubles of existence which determine this superiority?

Of small animals there are more sorts than there are of larger beasts: there are also more individuals of any one kind. Jeremiah appreciated the military advantages which would accrue if men could be as caterpillars: Leeuwenhoek, whose portrait so appropriately adorns the cover of the new American *Journal of Bacteriology*, said that there were more bacteria in one of his hollow teeth than there were men in Holland, and I know of no more precise data than such impressions of our common experience—a mighty treacherous guide. But it is uncommonly deceitful if we are wrong in thinking that there are more mice than foxes, more midges than horseflies, and generally many more little live things than big ones.

This numerical superiority of a small species is generally intensified by the parallel existence of a number of closely allied forms, each equally abundant, which are presumably more nearly equivalent in the economy of the world than the isolated large sorts with no very near relatives.

Associated with this larger prevalence is a larger activity in reproduction. From birth to maturity in an elephant may be thirty years, in a dog thirty months, in a rat thirty weeks, in a fly thirty days, in a bacillus thirty minutes.[2] What would have happened to knowledge if *Drosophila* bred as slowly as a sheep? Darwin pointed out that if you give elephants time enough they will come to be pretty abundant—nineteen million in 450 years is certainly multiplication. But if there had come from the ark just a pair of baby mice and a pair of baby elephants, the elephants would have been knee deep in mice[3] before anyone would think of giving them a copy of Dr. Stopes' guide. The soberest calculation raises a pair of rats to 200 in twelve months.

Let it be supposed that an infectious plague falls upon a population of n mice and $n/100$ or $n/1{,}000{,}000$ (whatever the fact may be) elephants. The results of the interaction of parasite and hosts must be presumed to vary in the normal way, which is one of the fundamental characteristics of measurable features of live things, either because of the doses of parasite being so distributed, or because the resistance of the recipient has this characteristic or for both reasons. The advantage of numerical superiority is plain; the larger the population the more individuals there will be who will survive by the possession of exceptionally large resistance or the reception of exceptionally small doses, or, if that be really a different thing, by being mutant in the right direction. The most resistant individuals of the larger population will also be more resistant than the best placed of the less abundant species, and this progressively with increase of numbers up to the limiting value (which is quite unknown). The mice then will be less likely to be annihilated, will have more survivors if there are any, and these will more quickly

[2] There are presumably pleasing mathematical relations between size, duration of life, maturity, length of pregnancy and so forth if only the data were available for analysis. A. Sutherland (Proc. Roy. Soc. Vict. VII (1895) 270) shows that the duration of pregnancy varies as the sixth root of the adult weight.

[3] Whether the mice would ever learn that elephants multiplied is a question which would have interested Samuel Butler.

reproduce the original community. Even if the small species is completely obliterated, there are others much of the same kind to replace it; but a rhinoceros will not do instead of an elephant.

The mice and elephants are indeed so differently situated with regard to infectious calamity that one may presume that their devices for meeting this particular kind of trouble are at least quantitatively different. An elephant has to protect the individual by developing its mechanism of resistance to parasitic invasion—it has, poor wretch, to acquaint itself with immunology; a mouse can let the individual go and trust to its numbers to get the species out of the difficulty. It would indeed be rather an excess of caution for a short-lived animal to take elaborate steps to protect itself against a repetition of an infection which recurs only occasionally. If, then, antibodies have anything to do with resistance, one may predict that elephants would yield sera of higher titre than mice. The final result of the mouse's tactics is also superior in that the properties on which it relies are in great part heritable, and the new population is on the average more resistant than the old one. The production of such immune races is fairly well established in man; in rats it was shown very clearly by the Plague Committee in India. Both species can develop individual resistance as well as antibodies, but such evidence as is available indicates that the rat is much less skilful in this than is man. The difference is quantitative, not qualitative.

When we come to organisms of the size and with the facility of multiplication of bacteria, it seems unnecessary to introduce any conception of acquired individual resistance at all. The establishment of resistant races is so quickly effected that nothing more is wanted, which is convenient, for there is not much room in a bacillus for any apparatus which can be dispensed with. What are the facts for invertebrates in general is not clearly known, but evidence of any mechanism for individual protection is, at the best, extremely scanty. The same appears to be true of the plant series: active resistance to the attacks of fungi and bacteria is absent or quite slight and, beyond such specialized tricks as discarding infected members altogether by shedding leaves, plants also seem to rely on their prodigious reproductive activity and the possession of various arrangements for preventing infection at their surface.

Active immunity, then, as human pathologists understand it, may have come to be important only in the latest development of the animal series: bacteria can be Darwinians, the larger mammals must be Lamarckians.

Small animals live faster, and in correlation have a shorter span of life, than their larger relations. Elephants live perhaps a couple of hundred years or so; the shrew-mouse is, to a considerable extent at any rate, an annual; the mice of the Imperial Cancer Research Fund die of old age in about two years: salmon live seven years or thereabouts; a small goby of two inches or so is born, breeds, and dies within twelve months. In proportion to its body weight a mouse uses, I daresay, about 100 times as much oxygen as an elephant; as Miss Buchanan has shown, its heart beats 800 times a minute instead of ten (which is a guess). How far this difference in the rate of metabolism holds for cold-blooded animals is rather uncertain; comparison is much more difficult than with mammals, but the data of Vernon, Mantuori, and others afford some evidence that a small fish or mollusc lives faster than a larger related species. It seems plainly true for invertebrates in general that the lesser sorts grow faster and attain maturity earlier, though the fact is apt to be obscured by their dependence on seasonal conditions. And it is a reasonable deduction that their rate of metabolism is higher.

Now this rapidity of life means that all the tissues can conduct their operations faster. The response to infection will be quicker in the smaller animals, the healing of injuries will not take so long. Suppose, for example, that a large and a small mammal are wounded and each loses the same proportion of their whole blood. The tissues of the small animal, including his red corpuscles, have the shorter span of normal life, and the apparatus for their manufacture normally has to produce the greater proportional output; hence when there is a call for active regeneration the new tissue will be made more expeditiously and the condition of anæmia resulting from the hæmorrhage will be more quickly healed.

It is a commonplace of palæontology that many phyletic series, vertebrate and invertebrate, beginning with smallish species, have progressed in size and complexity and then, at the summit of their development, have disappeared for ever. Hence the doctrine of extinction by gigantism on which geologists cheerfully predict that

the elephants, whales, and rhinoceros will go the way of the dreadful *Dinotherium*, likely by the road of the Martians. Man himself is a good deal larger than he was, and if he has not obviously grown in morphological complexity, he has added a good many detachable limbs to his equipment since he strewed our uplands with his bad shots at flint implements. It makes one feel rather nervous. I wonder if Augustine ever preached from *deposuit potentes*.

PAIN OF CENTRAL ORIGIN

By Gordon Holmes, C.M.G., M.D., London

IT is generally assumed that though injury, compression, and disease of peripheral nerves produce pain which is referred or projected to the peripheral distribution of the affected sensory fibres, lesions of the central nervous system run a painless course unless afferent roots are at the same time involved directly or by pressure. This assumption certainly accords with ordinary clinical experience; myelitis, encephalitis, and central inflammatory foci are not accompanied by pain except when the meninges are involved or when neighbouring sensory roots are affected, and tumours that invade or arise in the central nervous system cause pain only if they lead to an increase of intracranial pressure, or involve peripheral sensory fibres.

Thus the absence of peripherally projected pain is recognised as an important symptom in distinguishing intra-medullary tumours of the spinal cord from new growths which compress it; and when disease of the brain-stem or of the cerebral hemispheres is associated with pain referred to other portions of the body we naturally consider the possibility of coexisting lesions of sensory root fibres, or the presence of other morbid conditions, such as the joint and muscular changes that occur in hemiplegia.

The apparent insensitiveness of the central nervous system to disease and to mechanical stimuli has probably had considerable influence in the origin of many of the earlier theories on the function of the brain and spinal cord. Aristotle placed the central organ of sensation in the heart, and regarded the brain as an inert organ, since its mechanical stimulation in living animals did not appear to excite sensation. Similarly, in the eighteenth century, Lorry concluded that the brain could not be the central organ of sensation, as he found it insensitive to the coarse stimuli he employed. On the other hand, Haller, arguing from similar observations, expressed the opinion that the true *sensorium commune* must lie

in the deeper parts of the white matter of the brain and in the spinal cord, as it was only when these were injured that his experimental animals gave evidence of pain. Even in the last century Majendie came to the conclusion that as the brain is insensitive to pricking, tearing, cutting, and cauterisation it cannot be the seat of sensation.

But later experiences have shown that certain lesions of the central nervous system may be the origin of pain that is referred to the periphery, though these conditions are so infrequent that they may still be regarded as rarities in clinical medicine.

The most common cause of central pain is disease which involves the lateral and posterior parts of the optic thalamus and produces the thalamic syndrome that has been so accurately described by Dejerine and Roussy. This syndrome is characterised by persistent or paroxysmal pains, often of extreme severity and very intractable to treatment, which are generally described by the patient as sharp, burning, and lancinating, and may be referred to one half of the body or be limited to one region of the affected side. They are excited and aggravated by various external influences and particularly by such that normally produce discomfort. In fact, though apparently spontaneous, they are largely dependent on peripheral stimuli. As these pains are also frequently associated with over-reaction to stimuli that naturally excite sensations endowed with pleasurable feeling-tone, an over-reaction to all affective stimuli may be regarded as a characteristic feature of the condition.

From these and other facts Head and I, when working together, concluded that these peripherally projected pains are not, as had been generally assumed, due to irritation of central conducting tracts, but are a consequence of the removal of the inhibitory control which the cerebral cortex normally exerts on sub-cortical centres that are concerned in the perception of this form of sensation. We assumed that this centre lies in the inner division of the optic thalamus.

Practically the only other central lesion which produces similar pain is disease of the medulla oblongata and the lower part of the pons Varolii. In Mann's case, which has been frequently referred to in this connection, a lesion in the right half of the bulb was the cause of severe burning and shooting pains which persisted unabated

for years, throughout the left limbs and this side of the trunk, as well as in the right face. I have had under my care a man in whom disease of the same region caused similar pain.

During the late war I had the opportunity of seeing a very large number of men with spinal injuries and a few of these suffered with peripherally referred pains that could not be attributed wholly to irritation of sensory roots. I have collected the records of several such cases from among my notes, and as pain of medullary origin is certainly rare I venture to put forward some observations that I made by the bedside as evidence that in certain conditions pain may be due to disease of the spinal cord.

The variety of spinal injury in which peripherally referred pains are most commonly a prominent symptom is that due to gunshot wounds which produce concussion changes alone, or in addition slight direct injury, of the cervical enlargement. In such cases they may be a feature that transcends all other symptoms. They frequently radiate widely and diffusely through the arms and shoulders, and spread into the neck and across the upper part of the chest. When they are severe the patient can often not localise them more narrowly, but if less intense they may be limited to, or more constant and persistent in, one or other region, which, however, rarely corresponds approximately to the peripheral distribution of a dorsal root. They are generally described as burning, shooting, or stabbing, though it is not uncommon to meet even educated men who are quite unable to convey any idea of their nature by words. "Just one mass of pain, I can't tell you any more," one intelligent man remarked, while another after close questioning cried out petulantly, "It's as if knives heated in Hell's hottest corner were tearing me to pieces."

These pains are usually more or less constant, but they may be excited, and are increased, by all peripheral stimuli. Even the light contact of a finger or the touch of a wisp of cotton-wool evokes or aggravates them, but it is particularly movement of the affected parts that is dreaded by the patient; his arms invariably lie motionless, and any change of their position produces such agony that he fears to bring them into a more comfortable attitude. Even a slight jar to the bed may bring on a bout of intense pain, and if the condition is severe the patient may resent the step of a passer-by which

transmits an otherwise imperceptible vibration to it. I have not, I think, seen during more than four years' work in military hospitals, any condition associated with such intense suffering. Men with strong self-control who have borne themselves bravely through other experiences may break into tears and beg importunately for morphia, and more than one man I have known has prayed for death as a relief to the even temporary continuance of his intolerable sufferings.

But the suffering is fortunately only temporary, for as a rule the pains reach their maximum in the second or third day and begin to subside towards the end of the second or third week. At least, I know of no patient in whom they persisted unabated beyond a month or so after the infliction of the wound, and in several they had disappeared completely within this period.

When, as in such cases of cervical injury, the pains are limited to the areas of distribution of the cervical and upper thoracic nerves they may be, and in fact usually are, attributed to compression or irritation of the dorsal roots. But that this is not the only cause is made probable by several facts. In the first place their distribution is frequently so wide that it would be necessary to assume irritative injuries to a large number of roots, and frequently the nature of the wound makes this improbable; this argument is, however, partly discountenanced by the fact that concussion changes which I have previously described are frequently found in several pairs of dorsal roots above and below the level of the wound. In the second place the pains are frequently bilateral and equally severe on the two sides, even when the missile had passed to one side of the spinal cord; and finally, in certain of the cases that I was able to keep under observation I could detect no unequivocal evidence of injury of the sensory roots when the pain and tenderness has subsided sufficiently to permit a careful examination of sensibility.

But the strongest argument that it is not to irritation of the sensory roots that these pains are due is furnished by sixteen cases in which pains of similar nature were referred to distant regions of the body below the level of the wound. This interesting condition can be best described by the record of a typical case.

Case. Private M. was wounded on September 8, 1916, and was first seen by me seven days later. There was a small entry wound imme-

diately to the right of the seventh cervical spine and stereoscopic *x*-ray plates revealed a bullet in the apex of the right lung, as well as a fracture of the right lamina of the first thoracic vertebra, from which the missile had probably glanced off. He stated that immediately on receiving the wound both his legs became paralysed, but that he soon regained some power of movement in the left. His only sphincter trouble was a slight deficiency of vesical control and occasional incontinence of fæces, but these symptoms soon passed off. About seven hours after being wounded he began to suffer with severe pains in his legs, particularly in the right, which radiated up and down his limbs and were associated with a very painful stiffness and numbness "as if someone had been trying to break my legs." After the second day any passive movement of his limbs and every attempt on his part to move them evoked excruciating pain. When he was seen on the seventh day these pains were limited to his right side. Then all movements of his left leg were possible though weaker than normal, but the right limb was flaccid and powerless. The movements of his arms were unaffected, but voluntary, and respiratory expansions of the right side of his chest were smaller than those of the left, and the muscles of the right side of the abdomen were also paretic. His knee- and ankle-jerks were absent, the abdominal reflexes could not be elicited, and stimulation of the soles evoked extensor responses.

The most striking feature in his case were the pains in his right lower limb and in the right side of his trunk below the level of the costal margin. Even as he lay undisturbed in bed he suffered constantly with dull gnawing pains which seemed to creep up and down from his toes to his waist, and with a persistent aching as if his legs had been bruised or broken. In addition he had violent "shooting pains, like red-hot knives going through my leg," which darted from his foot or knee up to his abdomen and down again. When watched from a distance he could be frequently seen to clench his teeth, set his face and clutch the bedclothes in an attempt to control his reaction as a severe bout of pain seized him.

If his leg or trunk was touched the pains became "awful"; even when the bedclothes were gently raised he cried out in agony, "they are very sharp, I can't stand them," and the gentlest contact excited "sharp tingling and burning pains which run all over my leg, but they last only for the fraction of a second." Even shaking or jarring the bed gave him much discomfort, but it was rubbing or movement of the limb that produced the most intense suffering. Defæcation, too, was associated with much pain. "It's an awful pain to be moved," he said; "the pain goes into my right side and down my right leg; I dread it so much that it takes about an hour."

Examination of sensation revealed a complete loss of cutaneous pain, as tested by heavy pin-prick, in the whole of his left side below the third thoracic root area, as well as in the inner aspect of the right arm, and on a zone across the right side of his chest that corresponded to the cutaneous distribution of the second to the seventh thoracic sensory roots inclusive, but towards the upper and lower margins of this zone the loss was not complete (Fig. 1). Some pain could be, however, evoked by heavy pressure on the muscles and deep structures of the left leg. Tem-

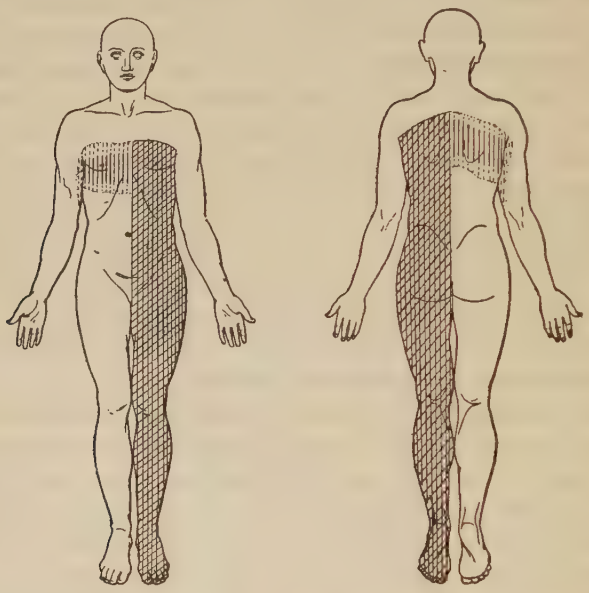

FIG. 1. THE VERTICAL LINES INDICATE THE REGIONS IN WHICH THERE WAS ANALGESIA; THE OBLIQUE LINES THE AREA IN WHICH THERMAL SENSIBILITY WAS LOST.

perature was not appreciated in any part of the left side below the fourth thoracic root area, but even mild degrees of heat and cold were recognised on the whole of the right side. The lightest tactile stimuli could be accurately perceived on both sides, but they were badly localised in the right leg. Finally the sense of position, the perception of passive movement and the appreciation of the vibrations of a heavy tuning fork were completely abolished on the right leg and on this side of his trunk.

Our patient consequently presented a characteristic Brown-Séquard syndrome, there being complete motor paralysis of the right side with pain and thermal sensibility abolished on the left, while the sense of position and passive movement, the appreciation of vibration and the locali-

sation of cutaneous stimuli were lost in the paralysed leg. There was in addition a zone of local analgesia in the areas of the right upper thoracic roots. Tactile sensibility was everywhere unaffected.

A careful examination of sensation in the right leg and in this side of the trunk revealed, however, important disturbances. Tactile stimuli, and especially moving ones, as rubbing with a wisp of cotton wool, at first evoked a sensation of intense cold, and later always produced tingling and pain below the level of the waist, while slight scraping or rubbing with the fingers excited considerable discomfort, or even "an awful pain that shoots up to my waist." Gentle pressure on the muscles or grasping the toes caused similar pain, but it was particularly movement of any joint of this limb that the patient feared. When sensibility to pain was tested by a sharp needle it was found that not only were the slightest pricks at once appreciated on the right side, but they evoked much more reaction and excited more pain than they did in normal parts; he complained that this pain "goes right through my leg," and that "when you prick my arm the pain stays where you touch it, but on my leg it runs up and down and spreads all over it." When, however, an algesimeter was employed no appreciable alteration of the threshold of sensibility to pain could be detected.

Thermal stimuli excited a similar over-reaction on the right leg; a test tube containing water at about 24° C. was "very cold, very painful, like ice; three times as cold as on my arm," and this was especially so when a massive stimulus was applied by a large vessel containing cold water. Similarly heat of even moderate degrees was "too hot, burning," but warmth (about 45° C.) was always "nice, very pleasant," and as far as it was possible to judge from his behaviour and descriptions it produced an undue degree of pleasurable sensation.

During the three weeks he remained under observation a considerable improvement took place. His left leg grew quite strong and its reflexes became normal again, and even with the right limb he was able to perform slight movements, though these required much effort and were much restricted owing to the severe pains they excited. The sensory disturbances, however, remained unaltered and all stimuli to the right side still produced excessive pain and over-reaction. The spontaneous pains in the right side also diminished considerably, and when he was transferred to England, four weeks after the infliction of the wound, the severer ones were limited to the region of his right knee.

This case is a fair example of the condition as I have observed it in a considerable number of patients. In the majority of those in

whom the point was specifically noted the pains commenced immediately or within a short time of being wounded, but in a few, as in Private M., not till some hours later, and three asserted that they suffered no unnatural discomfort till the second or third day.

In all the cases of this series pains occurred spontaneously and apart from any external stimulation, as far as it was possible to avoid this; indeed none of the various measures devised to reduce or abolish peripheral excitement succeeded in relieving the patients appreciably. On the other hand there could be no doubt that the suffering was much aggravated, and other pains were excited, by various external stimuli, and not necessarily by such alone that are capable of exciting pain or discomfort, or are endowed with feeling-tone of the unpleasant order. Thus not only pin-pricks, heavy pressure, high and low degrees of temperature, scraping and other such stimuli which are naturally unpleasant, but even the lightest touch or the slightest movement of the affected limb was dreaded by the patient. In certain cases, in fact, as in that recorded here, it was particularly movement that gave the greatest distress, so much so that early joint changes were frequently suspected, though examination and the later development of the condition disproved this hypothesis. Further, there could be no doubt that the movement itself, with the changes in the joints and the alteration in the tension of muscles around them that it entailed, was the main factor and not merely pressure on hypersensitive structures. It seemed, too, to be the rule that the mass or quantity of the stimulus was more important than its intensity; a light contact that moved over the surface, a moderate degree of pressure by the whole hand, the application of a large area of either heat or cold, evoked more pain than similar stimuli of less bulk but greater intensity. Stimuli that were continued or repeated at short intervals were particularly effective, as though the summated sensations grew to a magnitude out of all proportion to the single excitations.

The spontaneous pains as a rule began to diminish in severity towards the end of the second or in the third week, and at this period some of the patients suffered discomfort only when touched, or moved, or otherwise stimulated, but in a few they persisted during the six or seven weeks that the men remained under obser-

vation. I have, however, never seen the unnatural tenderness that is always associated with the spontaneous pains disappear entirely, though it too became gradually less intense.

The nature and origin of these apparently spontaneous pains, which obviously cannot be attributed to irritation of sensory roots, is a matter of some interest. It is probable that by studying the objective sensory disturbances that are constantly associated with them we can but obtain an idea of the nature, severity, and site of the spinal lesions to which they are due.

In twelve of the cases with distant pains the symptoms corresponded more or less closely to the Brown-Séquard syndrome, that is, one lower limb only was paralysed, or was at least weaker than its fellow, while thermal and pain sensibility were lost on the opposite side, and the sense of position, the appreciation of passive movement and of vibration, and the localisation of stimuli were affected in the paralysed half of the body. The symptoms consequently indicated unilateral spinal lesions which had interrupted the long conduction paths on one side of the cord. In the other four cases the symptoms were bilateral and due to moderately slight injuries.

In all the unilateral cases the spontaneous pains were limited to the paralysed side, though two men stated that for short periods they had pains in both lower limbs, and one other suffered while under observation with discomfort or slight pain in the analgesic side, but in this case the analgesia was not complete. It was consequently the rule that persisting pains did not occur in the side on which there was more or less persistent loss of pain and thermal sensibility. On investigating sensation on the paralysed side it was discovered that in addition to disturbance of those forms of sensibility which, it is generally assumed, are conducted by the dorsal columns of the cord the reaction to other stimuli and the sensations evoked by them were much altered. Touch, pressure, and movement, as well as pricking, heat, and cold, all excited much discomfort or bouts of pain, which spread widely and were similar in nature to those that were apparently spontaneous. There was what is generally called a "hyperæsthesia" to all these stimuli. Now the afferent impressions excited by these stimuli pass mainly through the opposite ventro-lateral columns of the cord, and presumably it is here that the anatomical changes to which the pains are due

must be sought. This hypothesis is supported by the observation that when conduction through this column is interrupted, as it was on the paralysed sides in certain cases, pain did not occur on the opposite side of the body, or did not at least persist beyond the first few days.

The sensory abnormalities on the paralysed side also give us some indication of the nature of the lesion. In several cases, as in the one recorded here, the thresholds of tactile pain and thermal sensibility were unaltered, though these stimuli evoked so much discomfort; in a few instances, however, these thresholds were slightly raised, but when sensations were elicited they still produced an abnormal amount of pain and suffering. We must consequently conclude that the lesions of the contralateral sensory paths were not sufficiently severe to block or seriously impede conduction. The most striking feature revealed by the histological examination of spinal cords which have been slightly or indirectly damaged by gunshot wounds is the presence of diffuse and widespread changes of relatively mild degree. The cord is swollen and constricted by its inelastic pial sheath, and microscopical examination reveals minute hæmorrhages, extensive œdema, and a peculiar swelling of the axis cylinders, which become irregular in calibre and are often increased to several times their normal diameter.

There can be no doubt that these histological changes may not interrupt conduction in the white matter which they affect; the correlation of the clinical symptoms and the pathological findings of several cases has made this certain. That they may modify the impressions that pass through the affected fibres seems very probable, and it is to this that I attribute the alterations in the sensations evoked by stimuli in the hypersensitive regions. The so-called spontaneous pains, in so far as they are independent of peripheral excitements, are probably due to the irritative effects of these lesions of the conducting fibres; and the rarity of these pains probably depends on the infrequency of that type and degree of pathological change that can irritate the fibres and yet not block conduction through them. The early pains on the analgesic side of which a few of the patients complained were probably produced by similar irritation of the central ends of sensory fibres that were more severely injured, and they ceased when the supervening secondary degener-

ation blocked conduction from the source of irritation towards the higher centres.

It is a remarkable fact that anatomical changes of this type are more common and more pronounced in the cervical enlargement, when this is affected, than in any other region of the cord. The more common occurrence of these pains when the cervical cord is damaged is due to this fact.

Whether it is only lesions of the ventro-lateral columns of the cord, which normally conduct painful impressions to consciousness, that can excite peripherally referred pains raises points of considerable physiological interest. The other main afferent sensory tracts of the cord are formed by the undecussated fibres of the dorsal columns; according to the generally accepted view these contain a subsidiary path open to tactile impressions from the same side of the body and subserve the localisation of cutaneous stimuli, and in addition convey centralwards those impulses on which the sense of position, the recognition of passive movement, the appreciation of vibration, the discrimination of two simultaneous contacts (Weber's compasses) and the recognition of size, shape, and weight depend. Now all these impressions, apart from those of touch and vibration, are concerned with the purely discriminative aspects of sensation, and it seems unlikely that any modification of these could excite pain. But as in a few of my patients the application of a vibrating tuning-fork was painful or unpleasant or "like electricity," though there was no discomfort when the fork was still, it seems that lesions of the dorsal columns can produce analogous symptoms. The faulty localisation of cutaneous stimuli on the homolateral side that results from an affection of the dorsal columns may be mainly responsible for the wide radiation and vague reference of sensations that are evoked on this side.

The numerous varieties of stimuli by which pain can be produced suggests strongly that, at least when nerve fibres are injured, pain may not be due exclusively to impressions conveyed by the normal pain-conducting tracts. It is only necessary that stimulation of any form should be of sufficient intensity or mass, though the most severe discomfort is caused by prolonged or moving stimuli which seem to be summated until they acquire an intensity that produces much suffering.

The pains and hypersensitiveness in these cases resemble in many respects that seen in the thalamic syndrome. It is in this connection interesting that stimuli endowed with pleasurable feeling tone may also excite an excess of positive pleasure. In the case recorded here certain degrees of warmth were always very nice and pleasant, and in two other cases in wliich observations were made they unquestionably produced more pleasure than they did in normal parts.

NORMAL OLD AGE

By G. H. Savage, London

I NEED hardly repeat the many reassuring epigrams as to our being no older than our arteries or no older than we feel. Theoretically our tissues ought, if they behave properly, to replace decaying or useless parts as simply as the engineer repairs damages to his engines, but though this goes on for many years reasonably well, there is a time limit, and habits or surroundings interfere with the process, and decay or arrested repair results. First of all there is no doubt that heredity plays a very important part in longevity. I have often been struck by the fact that two of a family have lived to advanced years, yet one had been sober and the other intemperate.

Someone says that we begin to die as soon as we begin to live. This is rather a fanciful way of putting the fact that we are always changing. I find many authorities start old age at sixty; this is as arbitrary as starting spring in February. Yet from or about sixty there are certain evidences of weakening in most people, both in mind and body. As a very worthy old lady told me, "It was then time to learn my limitations." I am inclined to think, if one carefully considers oneself after sixty or after seventy, certain things are marked. First, sleep is not what it was. One takes longer to get off to sleep and more often wakes after shorter hours of sleep, waking often quite unrefreshed—in fact, in a restless state of mind. This restlessness is one of the most marked and trying signs of old age. There is difficulty in applying oneself, and we look with dissatisfaction at the work done. On the other hand, the tendency to have many irons in the fire may, for a time, mislead one to suppose that one is capable of doing more than one can.

The rereading "Cicero on Old Age" will show the good work done by old men, but there is no analysis of the mental capacity of these men, and I sought in vain for consolation in the book.

Restless energy, if one may still use the word energy for restless activity, leads very often to intolerance of opposition and general irritability. Even without any real mental disorder, this, in social life, may result in family jars and subsequent litigation, over mental capacity in a testator. Here, then, we have the disorders which are common with advancing years and often these are recognised by one's friends before discovery by oneself. I think few men over sixty are not conscious of a growing defect in power of registration. An early factor in recognising this condition is the frequent expression, "I know this or that, but I cannot give it a name." In the Club or in the street one meets and recognises people, but fails to recall the name at first. This is distressful, and I am constantly meeting people who are worried about it. Normally, one manages to cover one's ignorance in some way. I have had many examples of defective memory that has been temporary. I have seen a man about his will, and his lawyer and friends and I have been persuaded that he was of sound mind, memory, and understanding, and yet later he proved to have had no recollection of our interview, nor in fact was his will at all what he had intended it to be. Memory of kindly acts or of injuries may be lost or hidden.

Though it may be necessary to reduce one's work and also one's pleasures, premature retirement often leads to rapid reduction of ability. Habits of work establish certain organic relations, and even questionable habits are better than no occupation. I have seen many men who have retired from business to enjoy life, who have ended in finding life intolerable. So far, then, with advancing years one has to learn one's limitations and, at the same time, keep going. With age there is loss of power, and there may be apparent gain along some organic lines. I have met the dyspeptic of forty-five later taking bread and cheese and beer at eighty.

As to the senses, most men of seventy notice some defect of sight, or more markedly, of hearing. The common expression that one is getting a little deaf covers a good deal. The victim tries to conceal it, but a time comes when theatres are a bore and meetings an abomination, for with age one is considered to be in a position to speak on any subject if one attends a meeting, and to speak on a subject only partially heard leads to misunderstandings. The

power of walking decreases and the dislike to going upstairs is noteworthy.

As I mix with my fellows socially and at work, I cannot help noticing that there are plenty of men working, and with little evidence of any intellectual defect, at and over seventy years of age. Slowly and smoothly they are passing on to the placid end, and leaving more fragrant memories than if they had passed away in their vigour.

Dean Stanley heartened Lord Shaftesbury with these lines:

> "Give me the solid trunk, the aged stem,
> That rears its scant but glorious diadem,
> That still, thro' lightning flash and thundrous stroke,
> Retains its vital sap and heart of oak.
> Such gallant tree for me shall ever stand
> A great rock shadow in a weary land."

And so I leave a subject more personal to the writer than to the object of our admiration.

ON THE ACTION OF ELECTROLYTES ON THE CONDUCTIVITY OF BACTERIAL EMULSIONS

AND THEIR EFFECT ON THE RATE OF MIGRATION OF BACTERIA IN AN ELECTRIC FIELD

By C. Shearer, M.D. (McGill), M.A., D.Sc. (Cantab.), F.R.S., Clare College, Cambridge, Eng.

TO the bacteriologist the problem of the permeability of the bacterial cell to chemical substances presents many features of special interest. It is, of course, well known that singularly few bacteria produce true exotoxins, the majority forming endotoxins, but the conditions under which these endotoxins pass the cell wall are but slightly understood. In some instances it would seem that some form of autolysis enters in the matter to a considerable extent.

Again, the remarkable part played by capsule formation in the acquisition of virulence by many races of bacteria points to the importance of the capsule in lessening permeability and the adsorption of various substances by the cell surface. The capsule would seem to play a rôle similar to the action of one colloid on another in preventing aggregation and flocculation, and the notorious difficulty always experienced in agglutinating these forms amply supports this view. Any investigation, therefore, of the conditions that alter surface energy or the permeability of the bacterial cell is of wide interest on account of its general bearing on many questions of infection and immunity.

In the following experiments an attempt is made to throw some light upon the subject, by a method which has been applied with considerable success to the investigation of the same problem in the egg-cell and in plant tissues. This consists in applying the Kohlrausch method of measuring the conductivity of electrolytes to the determination of the resistance offered by bacterial emulsions in various salt solutions. It can be easily and rapidly carried out, and

the work of McClendon, (1) Gray, (2) and Osterhout, (3) have shown that it gives, in the case of the egg-cell and plant tissues, fairly uniform results. It was found difficult with bacteria to obtain, even with the thickest emulsions, resistances as high as those obtained by these authors. In the following experiments, therefore, it is possible that the failure to find the preliminary rise of resistance, in the case of $CaCl_2$, La, Ce, and other trivalent salts, may be due to the use of low resistances.

I need not go into the question of the merits of this method of determining permeability. In the case of plant tissues it has been considered and discussed by Osterhout. (4) Briefly there seems to be no doubt that the electrical current does pass through the cells, and not between them, and a special set of experiments have been made by Osterhout (5) which go far towards definitively settling this point.

If a thick creamy emulsion of the meningococcus or *B. coli* is made up in neutral Ringer's solution[1] (that is, one in which the sodium bicarbonate is left out), and the conductivity measured by means of a Wheatstone bridge and a conductivity cell, it is found that its resistance is more than treble that of the same solution without the bacteria; that is, that more than two-thirds of the resistance is due to the presence of the bacteria.

The following are the details of this experiment: A twenty-four-hour culture of the meningococcus or *B. coli* on trypagar (24–30) plates was washed off in a considerable quantity of Ringer's solution, centrifuged down, and rewashed several times to remove serum, or any salts derived from the culture medium. The centrifuged deposit was then made up to a standard strength in Ringer's solution, so that it was not too thick to be sucked up with a small pipette (the orifice of which was 4 mm. in diameter), transferred to a Hamburger cell, and its resistance determined. It was found that the resistance of such an emulsion, when measured under similar conditions of temperature and in the same cell, was fairly uniform. If sufficient care was taken to get the emulsion of the right thickness, resistances of 110 ohms could be fairly constantly obtained with the meningococcus, and much higher resistances with

[1] M/8 KCl—25 c.c.—0.0031 M.—0.024 per cent KCl.
M/8 $CaCl_2$—15 c.c.—0.00187 M.—0.020 per cent $CaCl_2$.
M/8 NaCl—1000 c.c.—0.12 M.—0.7 per cent NaCl.

B. coli, the same quantity of Ringer solution under the same conditions having about 26.7 ohms resistance. Thus, more than three-quarters of the total resistance is due to the presence of the bacteria. Dead bacteria offer no resistance. Emulsions of dead bacteria have the same resistance as that of the fluid in which they are placed. (If an emulsion of bacteria in Ringer's solution is killed by gentle heat (55° C.), or a drop of formalin, its resistance immediately falls to that of the Ringer's solution.) If, however, we make up the bacterial emulsion in pure NaCl instead of Ringer's solution, the NaCl employed having the same conductivity as that of Ringer's solution, i.e., one in which the resistance is 26.7 ohms (which does not differ very greatly from a 0.85 per cent NaCl solution), we obtain as in the case of the same emulsion in Ringer's solution, an initial resistance of 110 ohms. This gradually drops within a short time and at the end of thirty or forty minutes the emulsion now has the same conductivity as that of the sodium chloride solution without bacteria, i.e., 26.7 ohms.

Sodium Chloride Experiment

Temperature 25° C.[2]

Resistance constant of cell = 7.02×10^{-1}

1. Resistance neutral Ringer's solution..... 26.7 ohms
2. Resistance Type III. Meningococcoccus in Ringer's solution. 110 ohms
3. Resistance due to the presence of bacteria, 110–26.7..... 83.3 ohms
4. Resistance same emulsion in NaCl of the same conductivity as Ringer's solution after ten minutes, 90 ohms; fifteen minutes, 80 ohms; thirty-five minutes, 49 ohms; two hours, 28 ohms.
5. At the end of the experiment the emulsion was subcultured, no growth.

Thus pure sodium chloride of about the concentration as that present in the blood gradually destroys the resistance of the bacterial cell. If the bacteria are allowed to lie in this solution for several hours, it will be found that at the end of this time on subculture they are dead. If they are allowed to remain in the NaCl for a short time only and then transferred to neutral Ringer's solution

[2] All measurements refer, both in the conductivity and the U-tube experiments, to those taken in a thermostat tank, the temperature of which was kept constant to within 0.05° C. In the conductivity experiments the same cell with fixed electrodes was used throughout.

again, they immediately regain their normal resistance and grow freely on subculture.

If when the resistance of the bacterial emulsion has fallen in the NaCl solution, a little $CaCl_2$ is added, it again returns to its normal conductivity and suffers no injury. Thus we get the usual antagonistic action of $CaCl_2$ to NaCl.

Calcium Chloride Experiment

Temperature 25° C.

1. Resistance of Neutral Ringer's solution..... 26.7 ohms
2. Resistance emulsion of *B. coli* in Ringer's solution..... 120 ohms
3. Resistance due to the presence of bacteria.....120–26.7 = 93.3 ohms
4. Resistance same emulsion well washed in three changes of $CaCl_2$ of the same conductivity as Ringer's solution after ten minutes, 120 ohms; after twenty-five minutes, 119 ohms; after two hours, 111 ohms.
5. At end of experiment emulsion grew well on subculture.

It was found that KCl, $LiCl_2$ acted like NaCl in reducing resistance, while $BaCl_2$, $SrCl_2$, had no such action, but behaved like $CaCl_2$. All emulsions made up in $BaCl_2$, $SrCl_2$ and $CaCl_2$, having the same conductivity as Ringer's solution, showed little change in resistance on being kept in these solutions for a short time. It is clear, therefore, from these experiments with bacteria, as in the case of so many other plants and animals, the entrance of the ions of NaCl, KCl, LiCl into the cell is prevented by the presence of a very small quantity of $CaCl_2$ or $SrCl_2$.

The interest of these experiments consists in that they agree completely with the results obtained by Loeb, Osterhout, and a large number of other workers on animal and plant cells.

In *Laminaria*, Osterhout (6) finds that with $CaCl_2$, and also with $BaCl_2$ and $SrCl_2$, there is invariably a brief temporary rise in resistance when the plant is placed in these solutions, of the same conductivity as sea water, but this is followed by a gradual fall. With the bacterial cell no such preliminary rise can be distinguished, while the fall due to the toxic action of the solution is much delayed and slower.

Experiment Demonstrating the Antagonistic Action of $BaCl_2$ to NaCl

Temperature 25° C.

(*a*) To 100 c.c. NaCl of the same conductivity as Ringer's solution a few crystals of $BaCl_2$ were added until the resistance was 20 ohms.

(*b*) To 100 c.c. Ringer's solution distilled water was added till the resistance equaled 20 ohms.

1. Resistance of *B. coli* emulsion in (*b*) was 95 ohms.
2. Resistance due to presence of bacteria, 75 ohms.
3. Resistance of same emulsion of *B. coli* (*a*) after fifteen min., 95 ohms. Practically no change.

In view of the remarkable action of trivalent ions on artificial membranes as shown by the work of Perrin, (7) Girard (8) and Mines (9), and the action on the permeability of cell wall as shown by the work of Mines, Osterhout, and Gray, it is of great interest to consider their action on the bacterial cell.

While the trivalent positive ion of lanthanum nitrate brings about a rapid rise of resistance at first, followed by a gradual fall in *Laminaria*, according to Osterhout, (10) and in the echinoderm egg according to Gray, (11) when this salt is used in such dilution as not to affect the conductivity of the solution itself, no such marked action can be distinguished in the case of the bacterial cell. The resistance remains unchanged, until it finally begins to fall on account of the increasing strength of the salt added, or to the prolonged action of the solution on the germs.

Lanthanum Nitrate Experiment

Temperature 25° C.

1. Resistance neutral Ringer's solution..... 26.7 ohms
2. Resistance emulsion of Type II Meningococcus in Ringer. 98 ohms
3. Resistance due to presence of bacteria, $98 - 26.7 =$ ..... 71.3 ohms
4. Resistance same emulsion in 0.0005 M. La (NO_3) in Ringer's solution after ten minutes 98 ohms; twenty minutes 96 ohms; forty-five minutes 95 ohms; one hour 95 ohms.
5. The emulsion growing well on subculture at the end of experiment.

In the same way the positive trivalent ions of $CeCl_3$, neoyetterbium chloride, and the trivalent negative ions of sodium citrate, appear to have little action when applied in the concentrations used in these experiments, in increasing or, in the case of sodium

citrate, decreasing the resistance of the bacterial cell, in so far as it can be determined with bacterial emulsions.

CERIUM CHLORIDE EXPERIMENT

TEMPERATURE 25° C.

1. Resistance of neutral Ringer's solution..... 26.7 ohms
2. Resistance 0.0005 M. $CeCl_3$ in Ringer's solution..... 26.7 ohms
3. Resistance emulsion Type III. Meningococcus in Ringer.. 108 ohms
4. Resistance due to presence of bacteria, 108−26.7=..... 81.3 ohms
5. Resistance Type III. Meningococcus in 0.0005 M. $CeCl_3$ in Ringer's solution after ten minutes 106 ohms; fifteen minutes 106 ohms; thirty-five minutes 103 ohms; forty-five minutes 100 ohms; one hour 100 ohms.

Yet it would seem remarkable, in view of the enormous preliminary rise of resistance given by the echinoderm egg when placed in 0.00005 M. lanthanum nitrate or $CeCl_3$ solutions in sea water, that some similar rise should not be found with bacteria when a 0.0005 M. solution is used. All experiments, however, failed to show it, even when solid deposits were tested, using the electrodes employed by Gray and giving resistances in the case of *B. coli*, as high as 150–200 ohms. Nevertheless subsequent experiments with the U-tube will show that these salts profoundly modify the surface conditions in bacteria. There was the possibility that with bacteria their relatively enormous surface would render any rise in resistance so temporary that before the emulsion could be centrifuged down and the electrodes placed in position and the bridge reading made, it would be over and passed. To test this point, a few crystals of La $(NO_3)_3$ were added to a thick emulsion of *B. coli*, in the conductivity cell, while the bridge telephone was kept to the ear. No momentary rise, however, could be detected, the resistance in each case falling directly. It would seem that bacteria are normally in a state of maximum impermeability, and that this cannot be further increased by the addition of $CaCl_2$ or the positive trivalent salts.

One of the difficulties in experimenting with the positive trivalent salts on living bacteria is that they bring about agglutination and flocculation at such remarkably high dilutions. La flocculates most bacteria in any concentration greater than 0.0005 M., and actually flocculates spleen broth cultures at much higher dilutions, while in this respect Ce has even stronger powers.

In distinction to the absence of effect of the trivalent salts on bacteria, as demonstrated by the conductivity method, is the marked action of these salts, and especially lanthanum, in changing the rate of mobility of these cells in an electric field. This can be shown by the ultramicroscopic method, or more readily by the U-tube.

That practically all bacteria in aqueous solutions carry a negative charge and move to the anode in an electric field, has been repeatedly confirmed by numerous investigators since the original observations of Nisser and Freidmann, (12) and Teague and Buxton, (13) and Cernovodeanu. (14) What is of interest here is that this charge can be materially altered by various trivalent salts, especially La and Ce.

When the ultramicroscopic method is used the most satisfactory results are obtained when the type of electrode cell devised by Hardy is employed. In it an ample space is left at each end of the field to confine and localize the heating effect of the electrodes. The motion of the particles is observed in the narrow channel connecting these two chambers. The cell used held about 0.5 c.c. with the cover glass in place. The usual procedure was to fill the space at either end with a little Ringer's solution, and add a drop of a thin emulsion of bacteria to the connecting canal, between the chambers, and to place the cover glass in position. The direction and rate of movement of the bacteria was then readily followed under the microscope with dark ground illumination. The distance between the electrodes was 5 cm., a continuous current of 110 volts being used, its direction being reversed every fifteen or twenty seconds by means of a key.

Below are given the data of a set of observations of this kind.

MOVEMENT TO ANODE +	MOVEMENT TO CATHODE −
B. Coli in	
(1) Aq. des. +	(7) Ringer plus 3 drops 20% sod. citrate −
(2) NaCl +	(8) Same transferred to fresh Ringer −
(3) Ringer's solution +	(9) Same washed three times fresh Ringer +
(4) Ringer plus 1 drop + 0.0005 M. La. $(NO_3)_3$ very feeble	(10) Ringer plus 4 drops 0.0005 M. $CeCl_3$. −
(5) 0.01, M. HCl. +	
(6) 0.1, M. HCl. −	

It will be seen from the foregoing table that *B. coli*, in distilled water, NaCl, and Ringer's solution respectively, carry a negative charge and move to the anode. The addition of a slight trace of La or Ce to any of these solutions immediately slows up the rate of migration considerably. These salts when added in stronger strengths clearly reverse the direction of movement, the bacteria now passing to the cathode. That is the sign that their charge has been changed. Almost immediately flocculation supervenes, the bacilli clump and stick to the slide and show no further movement. It is difficult, for this reason, to confirm these results with the U-tube, and only in the case of HCl was this change demonstrable by both methods. *B. coli* in 0.01 M. HCl in Ringer's solution moved slowly towards the anode, while in a 0.1 M. solution it moved to the cathode. This result agrees very well with that obtained by Teague and Buxton (15) working with sensitised bacteria, the sensitiveness of which to the action of electrolytes is about double that of the untreated germs. They obtained a change in direction of motion with sensitised *B. pyocyaneus*, using a 0.01 M. HCl solution.

The ultramicroscopic method has, however, several drawbacks, first, on account of the rapidity with which the products formed at the electrodes and, second, heating effects interfere with the experiment; these quickly render the movements irregular and obscure the real direction of motion, sometimes reversing it entirely.

These difficulties are avoided to some extent when the U-tube is used. The particular type of instrument employed in the following experiments was that devised by Hardy. (16) It is provided with a funnel permanently attached, and both limbs are graduated in millimetres. It was found that the movement of bacteria in it could be readily measured under a potential gradient with more accuracy and uniformity than by the former method. In the following tables the data of a number of measurements obtained with it are given.

If, in the terms of the Helmholtz-Lamb theory of the double electric layer, we regard the surface tension of the bacterial cell in a solution as the balance between the cohesive force of the cytoplasm and the disruptive force due to a layer of negatively charged anions attached to the cell surface, the corresponding positive ions being held by the surrounding solution, then the determination of the electric moment due to this charged state can be simply estimated

by measuring the velocity with which the bacteria wander towards the anode in an electric field.

If we make use of Perrin's (17) formula, $\sigma H = n\frac{v}{d}$,
where σ = density of electric layer on the bacteria;
H = strength of electric field:
n = coefficient of viscosity;
d = distance between the double electric layer,
we have $\sigma d = \frac{nv}{H}$, which gives us the value of the electric moment for bacteria in any solution.

The following table furnishes the data from which the value of σd for several strengths of La can be readily calculated. They show how easily the value σd can be changed or modified by very dilute solutions of the positive trivalent salts.

Emulsion *B. coli* in Spleen Broth
Distance between electrodes 32.5 cm.

Time	Voltage Sign Right Electrode	Temperature	Height Bacterial Emulsion		Observed Velocity in cm. sec.
			Left Limb Tube	Right Limb Tube	
(1)	+110	25° C.	2·5 cm.*	2·5 cm.	
5 min. int.	+110	25° C.	2·4 cm.	2·7 cm.	
	+110	25° C.	2·4 cm.	3·0 cm.	
	+110	25° C.	2·3 cm.	3·1 cm.	
	+110	25° C.	2·1 cm.	3·1 cm.	4.17×10^{-4}
1 c.c. of 0.0005 M. $La(NO_3)_3$ added to 10 c.c., same *B. coli* emulsion.					
	−110	25° C.	1·6 cm.	1·8 cm.	
5 min. int.	−110	25° C.	1·5 cm.	2·0 cm.	
	−110	25° C.	1·5 cm.	2·2 cm.	
	−110	25° C.	1·5 cm.	2·3 cm.	
	−110	25° C.	1·5 cm.	2·4 cm.	2.92×10^{-4}
Current reversed.					
(2)	+110	25° C.	1·5 cm.	2·3 cm.	
5 min. int.	+110	25° C.	1·6 cm.	2·2 cm.	
	+110	25° C.	1·9 cm.	2·1 cm.	
	+110	25° C.	1·9 cm.	2·1 cm.	
	+110	25° C.	2·0 cm.	2·1 cm.	2.92×10^{-4}

* Limbs of the tube numbered from the bottom.

If 10 c.c. of a thick growth of *B. coli* in spleen broth be run into a U-tube under neutral Ringer's solution of the same conductivity as the broth, then on passing an electric current through the tube, the temperature being constant, an even and rapid migration of the bacteria takes place towards the anode, the observed velocity being 4.17×10^{-4} cm. per second.

If, now, to this 10 c.c. broth culture 1 c.c. of a 0.0005 M. lan-

thanum nitrate solution is added, it will be seen from the table that the rate of migration is now 2.92×10^{-4}; that is, the La has slowed the rate of movement by half. It was found that the addition of the La to the broth made little appreciable difference in its viscosity, this being 11.69×10^{-3} without and with the La. If 2 c.c. of the same La was added to 10 c.c. broth culture, no movement could be observed, the isoelectric point being reached and flocculation took place.

If we substitute these values in Perrin's formula—$\sigma d = n_H^V$ we get the following evaluation of $\sigma d = 1.45 \times 10^{-6}$ in the above experiment for the broth without La, while we get for the same broth culture plus the La $\sigma d = 1.02 \times 10^{-6}$ per cm. per sec. per volt per cm.[3]

Thus we can materially alter the surface energy conditions of the bacterial cell with weak solutions of the trivalent positive salts, although these changes are not distinguishable by the conductivity method.

Summary. 1. The results of the foregoing experiments show that living bacteria, as distinguished from dead, offer considerable resistance to the passage of ions of various salts. Dead bacterial protoplasm offers no resistance to the passage of these ions. There is something peculiar to the living state that conditions this resistance. This essential difference between dead and living cells should be kept in mind in all our application of the results of protein chemistry to living protoplasm.

2. The conductivity of thick emulsions of the meningococcus or *B. coli* show that this is altered by electrolytes in a very characteristic manner. The important part in this alteration is played by the cation. All monovalent cations, such as Na, K, Li, Cs, Rb, produce an increase in permeability of the bacterial cell. This is at first reversible, but if allowed to follow its due course leads to complete permeability and death. Bivalent cations such as Ca, Sr, and Ba, on the other hand, lead to an irreversible increase in permeability which finally becomes complete with death after some considerable time.

3. Small amounts of the second group of salts can be added to the first, so as completely to antagonise their action, when a balanced solution results in which no change of permeability takes place.

4. The action of the trivalent positive salts on bacteria is very marked. The addition of 1 c.c. of a 0.0005 M. lanthanum nitrate solution to 10 c.c. of bacterial emulsion in spleen broth was sufficient almost to double their surface tension.

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[3] Observations of a nature somewhat similar to the above, using the same formula, have been recently recorded by Girard and Audubert (*Compt. rend.*, 1918, CLXVII, 351), but they have given no data as to the methods used or the strengths of solutions adopted. They record remarkable growth changes due to the action the trivalent salts, especially lanthanum, on various bacteria.

NOTE ON THE HISTORY OF THE WORD "TONUS" AS A PHYSIOLOGICAL TERM

By C. S. Sherrington, Oxford

IN contributing to this volume, dedicated to one who has done so much for the study of the history of medicine, I have thought that a note, imperfect though it be, on the vicissitudes through which a biological term has passed might have especial appropriateness of endeavour.

The term *tonus*, as met with in physiology and medicine, is often complained of as lacking the precision and clearness which are desiderata for a technical term. That it is vague and applied with various meanings to very different phenomena is notorious. It embraces muscles and nerves and nerve-centres. Besides mechanical tonus we read of chemical tonus. Under "bio-tonus" is understood a particular view of the metabolism of cells in general. To quote a recent writer, Matula (1913): "Each author understands by the term something different, and usually each is unable to supply any sharp definition of the conception."

It is of the term tonus in its application to muscle that this sketch proposes to treat. In Galen we find the word employed in several senses. Among these uses is that of ὁ τῶν μυῶν τόνος; that is the technical use of which the following outline would attempt to follow the subsequent history.

If we turn to Galen "On the Movement of Muscles," we see (Bk. I, cap. VII and VIII) that he distinguishes four kinds of movement exhibited by them: (1) contraction, (2) lengthening, due to contraction of the antagonist muscle, (3) passive movement, as when the arm drops to the side under its own weight, (4) the "movement" obtaining when, for instance, the arm having been raised by its muscles is then retained in the raised position and prevented from falling. Galen says that, though in this last case there is no gross movement, he considers that there is really in essence a motion, and that such states are τονικαὶ κινήσεις, tonic actions.

He adds, it matters little whether one calls them "tonic" or something else; the point of importance is that there exists a (muscular) activity of the kind described. We notice how foreign the modern idea of "work" is from Galen's more naïve view; also that his fourth kind of muscular movement, his tonic action, is what we should now speak of as "active posture." It is perhaps hardly permissible to pass at a stride across fifteen successive centuries, but turning from Galen to the "De loc. mot. animalium" of Fabricius we find the word "tonic" reappearing with practically no alteration of its above meaning. Under "De Gressu" we read:

"Let us see how the legs behave in standing. When both legs stand although there is in them no visible motion of the muscles, all the muscles are of a truth in motion and in action. And this motion, unapparent though it is, is rightly designated by the term tonic, τείνω, in Greek, which would say tense. . . . For the motion is tonic by which the arm or leg or other member is maintained tense in virtue of all the muscles whether flexors or extensors operating in it have been drawn in the above sense tight."

And then and in other places he speaks of the relatively great exhaustion ensuing on tonic action, not discriminating, for how should he at that date, between reflex action and willed effort, and not envisaging the possibility that the fatigue is of nerve centres and not of muscles. And there is an odd passage where he seems to depart somewhat from the Alexandrian meaning of the term:

"And so if no muscle act the body is always imbecillum; if few act a small strength is exerted, if many, much; if all, as in tonic motion, the body obtains the greatest, the whole, strength; and everywhere."

Yet, on the whole, the word retains in his use of it, the meaning "active posture" as in Galen's text.

Much later in the same century one meets the term in Borelli's "De Motu Animalium" (Rome, 1680); not, it is true, *motus tonicus*, but *actio tonica*. With the like meaning, however, and chiefly instanced by the same example, standing. There is an advance in the analysis of the posture. "Therefore the falling forward is prevented solely by the extensor muscles, and not in fact by the tonic action of extensors and flexors operating concurrently."

"Therefore men do not maintain station by the tonic action of all the antagonistic muscles, but by the operation of all the extensor muscles and some of the flexors, while some of the flexors remain inoperatively at rest" (Lib. I, prop. CXXXVI); an approximation toward the modern view. And it is clear that for Borelli the term "tonic" still conveyed "postural." In short, the word had lived without change for nearly sixteen centuries, and even a century of the Renaissance had not surcharged it with more, or at least with altered, meaning. But the Renaissance as regards biology is the latest of all chapters of the Renaissance, because analytic as apart from merely descriptive biology had to wait for the rebirth of physics and chemistry before it could find itself.

It is significant, therefore, that from a chemist, who was also a physician and physiologist, sprang, so far as I can trace, the first main departure of tonus from its previous path of meaning. In Stahl's writings it becomes one of the shibboleths of that doctrine of vitalism which his name chiefly represents. With Stahl tonus is a sort of touchstone for life itself. How this position arose is perhaps best gathered by turning back to Francis Glisson. Stahl's "Dissertatio de motu tonico vitali" appeared in 1692. Glisson in his "Tractatus de natura substantiæ energetica, 16—," had dealt penetratingly, though with a terminology that to us seems obscure, with what we should now speak of as the excitability of tissues. The fundamental factor in this excitability he attributed to the *perceptio*. He distinguished from other species of *perceptio* a *perceptio vitalis* of the tissues, equivalent broadly to what to-day is known as the direct excitability of tissue, i.e., in response to artificial stimuli applied to it directly. He showed that the intestine and the muscles even after removal from the body exhibit movement in response to certain agents acting on them. Such reactions were the evidence of his *perceptio vitalis*. One development of Glisson's theme culminated in the next century in Haller's investigation of the irritability of skeletal muscle, or "muscle," as it was then called, for not until much later was "smooth muscle" considered to be or included along with "muscle." As regards muscle in that older sense of the word, Haller in the eighteenth century established as a concrete example of *perceptio vitalis* the property which he termed "irritability," but which we know to-day as "contractility."

The defect in his analysis is from the modern standpoint that he did not sufficiently realise that the contraction is only the end link in a chain of events between stimulus and final reaction. But it was in other tissues than in muscle, using that term in its old sense, that the chief interest of the problem lay for Stahl and the vitalists. They were intent to show, *inter alia*, that every part and parcel of the animal structure is imbued with an immanent vital principle, and that every one of them possesses in Glisson's phrase *perceptio vitalis*. Movement with them, as with others, was of itself suggestive of life. The reactive movement of pieces of viscera, arteries, skin were exhibitions of the vital principle inhering even in excised and mutilated fragments of the body; they were exhibitions of "*motus tonicus* essential to and inalienable from the maintenance of life" (Stahl, 1696). "*Motus tonicus* is essential for life." They accepted even the shrinking of pieces of intestine or blood-vessel or skin under the action of corrosive fluids or of the hot iron as evidence of *motus tonicus*. Their critics pointed out the weakness of some of their evidence: that leather, for instance, as so judged evinced *motus tonicus*. The opposed view was that elasticity of non-vital nature explained the *motus tonicus* and was no evidence of inherent life. Bordeu of Montpellier argued in the same way as Stahl. Barthez, his pupil, wrote of *des forces toniques* in the same sense. Robert Whytt, whose work on the muscles and nervous system, apart from Haller's, is the most remarkable of the eighteenth century, does not, so far as my search in his writings goes, mention the terms tonus or tonic, although he describes what we call now active posture. He was, of course, opposed to the "vitalists" of his time. It seems to me likely that he eschewed using the word "tonic" because it had become, so to say, part of the armamentarium of Stahl and Bordeu and the vitalists. The essence of the controversy, as seen from this distance of time, was as to whether in these "fibrous" tissues—and "plain muscular tissue" was at that epoch not clearly discriminated from fibrous connective tissue—such reactions as those mentioned above were evidence of life or not. At the opening of the nineteenth century Bichat, in the "Recherches sur la vie et la mort," dealt with the subject, but, like Whytt in the preceding generation, he seems to avoid using the word. With him the term employed is *contractilité organique insensible*, or in

other passages, *contractilité par défault de extension*, or more rarely *contractilité de tissu*. We note the gain in lucidity, especially in the second of the above phrases. But the controversy was dying down; its interest waning, as the medley of disparate observations, at first jumbled together, in due course became sorted by more adequate experiment and resolved in the one sense or in the other. We find "elasticity" the preponderant dictum on the subject in Bostock's "Elementary System of Physiology," London, 1824; and a short critical couple of pages to the subject under the heading "Tonus," in Vol. I of Tiedemann's "Handbuch" of 1830. Tonus with its old connotation of posture seemed to have lapsed from use. A little later a new phase, however, opened for the word. The Philosophical Transactions of 1833 contain one of Marshall Hall's earlier papers, "The Reflex Functions of the Medulla Oblongata et Spinalis." In describing the state of the muscles after severance of the spinal cord, especially as seen in amphibia and reptiles, he speaks of "the tone of the limbs," "the tone of the sphincters." Three years later, in his lectures on the Nervous System, London, 1836, he writes (p. 26), "the whole tone of the muscular system is the result of an excito-motory function." For him the term "excito-motory" is equivalent to "reflex." This seems the first definite announcement of reflex muscular tonus; and he makes it embrace not only the skeletal muscles, but certain smooth muscles, the sphincters, also.

In 1841 appeared, as a volume of Soemmering's "Bau des menschlichen Körpers," Henle's "Allgemeine Anatomie; Lehre von den Mischungs und Formbestandttheilen des menschlichen Körpers." It will be remembered that Henle had been associated with Schwann and Schleiden, in J. Müller's laboratory, in the founding of the cell-theory, though the announcement had been first actually proclaimed by Schwann and Schleiden. The conception of smooth muscle, as we now have it, was largely the work of Henle. In his "Allgemeine Anatomie" he is very explicit about tonus.

"Under the name tonus one understands the moderate tension of the contractile fibres which is considered a physical property. After it has now become known that this tension is maintained by the nervous system and is therefore based upon the activity of the latter it has become admissible to shift the term tonus from the contraction to the nervous

force which brings about the contraction. . . . I will call the moderate grade of activity in the nerves during their so-called rest the tonus of the nervous system. Thereby I extend to the entire nervous system a conception which has long been accepted indirectly for a part of that system, namely the nerves of muscles."

When the nerve is cut, tonus and excitability of muscle disappears. When the spinal cord is transected, the nerves retaining their attachment to the cord, tonus and excitability remain; therefore tonus comes from the grey substance of the spinal cord whence the nerves derive. The nerve-matter is never at rest. The content of the nerve-fibre is "always oscillating, like the cilia of an epithelial cell, so long as it lives." This continual moderate nervous activity or tonus is independent of external causes; it is internal in origin. Such are Henle's statements; a generalisation giving tonus much the same scope as Marshall Hall's, but making the word more figurative by applying it to the nervous system, thus dropping all semblance to mechanical tension. Also there is the further resemblance and difference that Marshall Hall declared the tonus to be reflex, although he gave no proof that it was so, while Henle as confidently declared it to be autochthonous and not reflex, although he gave no proof that it was not reflex. It is, however, of some interest, as bearing on the connection between the physiological and more generally medical and popular connotations of the term, to follow him briefly in a psychological excursus which he allows himself:

"This power 'tonus' is dependent on the action of the grey matter, and in that matter directly upon the nutritive material supplied by the arterial blood. It disappears at once on stoppage of the circulation and varies pretty closely with the richness of the blood in nutrient material. The tonus is essentially different in different individuals. Upon it chiefly is founded the differentiation between different temperaments; under accidental circumstances it can for longer or shorter times be altered in one and the same individual, hence the foundation of mood. . . . I said that the differences of temperament and mood correspond with grades of tonus in the nervous system. Our diagnosis of temperament turns on the amount of contraction obtaining in the resting muscles, especially those of the face."

The whole passage with its mingled shrewdness of characterisation and shallow crudity of explanation is reminiscent of some pre-renaissance page.

In the 1844 issue of John Müller's "Handbuch der Physiologie" there is more reference to tonus than in the first (1834–1840). Henle was Müller's pupil; the view given resembles that cited above from Henle—a moderate steady contraction of all muscles always going on even when the muscles are said to be at rest. No biological purpose is ascribed to this tonus. It is derived from the nerve-centres, but whether of reflex origin in them or whether autochthonous, Müller does not explicitly state. It has become a somewhat mysterious property of the nervous system, the expression by the whole musculature of an unceasing generation of "nervous force" by the nerve-centres, perhaps in virtue of their very life.

Then for the next twenty years follow papers enquiring into the all-pervading tonus of nerve-muscular system, some by noteworthy names—Auerbach, Heidenhain, Schwalbe, Stilling, Pflüger. The plan in general was to look with telescope or kathetometer for a slight elongation of the muscle (frog) ensuent on severance of the muscle's nerve. Divergent results were obtained, by some slight lengthening, by others none. The very existence of a tonus of skeletal muscle became a matter of doubt. But in 1860 Brondgeest of Utrecht furnished his experimental proof of a reflex tonus in the hind-limb muscles of the frog. The supporting centripetal impulses ran *via* the dorsal spinal roots of the limb itself; but whence, whether from the skin or whether through all the afferent fibres or through some only, and if so, which, remained undetermined. In 1871 we find Eckhardt, an acute critic and versed in the history of the experimental study of the nervous system, posing the question whether the belief in a reflex tonus of all muscles and at all times were really well-founded. And it is noteworthy that no purposive function of tonus for the economy of the organism is explicitly or even implicitly referred to; nor had it been, so far as my acquaintance with the literature reaches, for more than a hundred years past.

It is unnecessary here to follow the history of the term during the past forty years, except to add that the last two decades have seen an interesting reversion of its meaning to the original one carried in the passage quoted from Galen at the outset of this note. The term possesses now, with a precision and basis of fact hitherto wanting to it, its pristine significance of "active posture." But this return to its old Alexandrian and Renaissance use has come

about without thought on the part of those who have brought it about that in their pages there is re-embodied the very notion which it possessed so long ago. The history of a word often epitomises the discussions and questionings of the generations that have used it. This is, of course, less true of words used as mere technical terms than of words in common use in the general literature and the everyday speech of the people. In the mere technical term there is little chance for flavourings of humour or pathos or even for the passing mannerisms of an age. Yet the vicissitudes of meaning of the word tonus as a technical term in physiology do mirror in a not unstriking way phases of the story of the science. Starting with clear descriptive scope in the Greek school at Alexandria, passing through fourteen centuries without change, as it were in suspended animation, to enter at last the turbulence of the Renaissance and then become metamorphosed to something like the shibboleth of a creed in the writings of the early eighteenth century vitalists, recovering from that to stand for a mysterious neuromuscular principle through the first seventy years of the nineteenth century, and now in the twentieth reassuming with added precision and analytic depth the significance it had in Galen's employment of it seventeen centuries ago.

THINKING AND DREAMING AND THE EXPLANATION OF DREAMS

By F. Parkes Weber, M.A., M.D., F.R.C.P., London

THINKING and dreaming! How easily the one passes into the other! Our thoughts begin to "wander" when we are tired, or when we allow our minds to enter into a reverie or day-dream or to "build castles in the air." When we are tired out over literary or other work, necessitating much and long-continued efforts of our reasoning faculties, our thoughts tend at last to "wander"—the voluntary, directed, objective efforts of the fully conscious mind give way to the easy, swiftly flowing, objectless, but usually pleasurable, play of fantasy—heralding the approach of a state of subconsciousness and the overpowering onset of deep sleep and complete unconsciousness.

So also I believe that the unconsciousness which often comes before death is not rarely preceded by a dream-like state of the mind—a condition free from pain, which may be an actually pleasurable one of mental euphoria. In exhausted and toxic conditions (septic fevers, etc.) of the body the mind is indeed often mercifully allowed to "wander," and an easy dream-like subconscious state of mental fantasy or a "busy," but mostly not unhappy, delirium succeeds the conscious pain, malaise, or wretchedness of grave disease.

The visual and auditory hallucinations and delusions in severe diseases, toxic conditions (delirium tremens, etc.), and various forms of insanity are *pathological* dream-like phenomena, resembling ordinary, more or less *physiological*, dreams in being unrestrained by the higher psychical controlling mechanism (that is to say, by the normal mind). They consist, like ordinary dreams, of a series of images and sensations running riot—for example, the kaleidoscopic (often *kak*eidoscopic) ever-changing hallucinations and delusions of delirium tremens. The difference between the more or less normal phenomena of ordinary dreaming and the pathological

phenomena of such hallucinations and delusions is that in the former it is only the borderland between the fully conscious and the unconscious regions of the mind that is concerned, whereas in the latter the whole mental field may be involved, for the higher portion has undergone a (probably only temporary) regressive change so as to have become reduced to the condition of the subconscious mind.

On every side, and from whichever way we look at it, thinking passes gradually into dreaming—or rather, the fully conscious, objective and reasoning effort of thinking falls to a lower semiconscious, easily flowing and unrestrained "play of thought," which tends to become more and more fanciful as it gradually passes altogether out of the limits of voluntary control. Such dream-like thought doubtless represents the mode of thinking characteristic of our infancy, and of our remote ancestry (the childhood of the whole human race), and (probably to some extent also) of animals.

Allowing the thoughts to "wander," the phenomena of reverie, day-dreams, and "building castles in the air," furnish us with the connecting links between the normal adult mode of thinking on the one hand, and true dreaming on the other. Some young (and even older) persons fall more readily than others into a habit of day-dreaming, and building castles in the air, and many of them must indeed welcome their day-dreams and gladly seek to indulge a habit which gives them pleasure and fairy-like delights as compensation for the hard realities of their actual life's experience.

In true dreaming during sleep—generally preceding the onset of deep (completely unconscious) sleep, or heralding the return to wakefulness—voluntary control of the thoughts is entirely absent, and the mind runs its own subconscious course, free from the (sometimes rather irksome) fetters of reason and conscience, and unguided by its own god-like will-power. Reversion to the primitive dream-like method of thought may be beneficial, even when undesired, and often comes as a relief to mortals exhausted by fatigue, shock or disease. In fact, effortless dream-thought may be restful to the mind, just as intervals of ease and sleep are refreshing to the body.

C. J. Jung, of Zürich, insists that the comparison of the themes of dreams with those of myths (mythology) suggests the idea—

as explained by Nietzsche and Freud (1)—that from a phylogenetic point of view dream-thought is a regressive phenomenon and should be regarded as an older form of thought, in fact, that dreaming represents the survival of a kind of childish (infantile) or ancestral mode of thinking. How well Nietzsche (2) expressed this idea is shown by the following quotation given by Jung: (3)

"In our sleep and in our dreams we pass through the whole thought of earlier humanity. I mean, in the same way that man reasons in his dreams, he reasoned when in the waking state many thousands of years. . . . The dream carries us back into earlier states of human culture, and affords us a means of understanding it better. The dream-thought is so easy to us now. . . . To a certain extent the dream is a restorative for the brain, which during the day is called upon to meet the severe demands for trained thought, made by the conditions of a higher civilisation. From these facts we can understand how lately more acute logical thinking—the taking seriously of cause and effect—has been developed; when our functions of reason and intelligence still reach back involuntarily to those primitive forms of conclusion."

Of the two modes of thought Jung points out (4) that modern adult trained thought (directed thinking), working for communication with speech elements, is troublesome and exhausting, whereas dream-thought (the infantile or ancestral mode of thought) goes on without trouble, working spontaneously with reminiscences.

Nothing seems to me (F. P. W.) better able to illustrate and contrast the two main classes (conscious and subconscious) of thought than the following considerations on mental preoccupation from the psycho-analytical point of view. When a person's mind is preoccupied by anxieties, regrets or disagreeable ideas, there is a desire to go back—"retire into oneself," search one's mind, and analyse the disquieting elements in it (vague and almost subconscious though they may be). It is difficult to readily "collect one's thoughts" for the immediate work before one—one wishes to clear the mind first, in order to start afresh on the ordinary practical business of one's daily life. When immediate work is very urgent, however, and one has to do it, one may succeed in driving back the disturbing elements into the subconscious regions of the mind. Even then one's mind does not work normally, rapidly and smoothly as it generally does in most persons—"the machinery wants oiling"—or, as in telephonic language—"the junctions are engaged" just when one wants to use

them. Clearly, in the mental processes employed for ordinary voluntary work the subconscious part of the mind plays a part—probably an important connecting part, as if it were a region through which the "*wires* of telephonic communication" have to pass, *by means of which* the "voluntary run of one's thoughts" is facilitated, checked, and "fed" or "nourished" and embellished (that is to say, with the memory or subconscious memory of experiences or of what one has witnessed, heard or read of).

Ordinary experience seems to me (5) to explain dreams (from another point of view) as hallucinations (visual, auditory, etc.)—or rather, as a series of images and sensations—presenting themselves to the subconscious mind, or the border ("twilight") region between unconsciousness and complete consciousness—founded on or suggested by incidents, impressions, or thoughts in the dreamer's previous, generally quite recent, life—often disturbed, disconnected, or fantastic, owing to the necessary absence of control by the higher conscious mind (the psychical controlling mechanism), and often, therefore, untrue to life and opposed to the dreamer's character, at least, to his actions when under the guidance and control of his conscious mind. Bergson pointed out that dreams result from "relaxed consciousness"—in other words, they result owing to the working of the mind becoming temporarily regressive, trained (directed), conscious (wakeful) thought giving place to the easier (flowing) "ancestral" dream-thought. It is no wonder, therefore, that what a person during sleep dreams that he does (his action in his dreams) is often out of keeping with what is known of his previous life.

If the above-stated conception of the nature of dreams be admitted, how can one support the Freudian claims that nearly all dreams allow of an obvious or latent (cryptic) sexual interpretation? Such teaching seems opposed both to theory and to common experience, and in fact to be preposterous. In ordinary thought a sexual character is only occasionally present—why should it invariably be present in dream-thought? Most persons ordinarily think and dream (if they know that they have any dreams at all) about matters which have nothing specially to do with sex. One might just as well seek to explain all the fancies and hallucinations of delirium tremens and all the delirious ideas and delusions of fevers and acute mania as if they always rested on a sexual basis.

In many cases the correct source or starting-point of dreams can readily be found in the dreamer's previous experiences, what he has done, witnessed, listened to, been told of, read of, thought of, approved of, disapproved of, or discussed; that is to say, in his previous (generally recent) life. But the bulk of ordinary emotions in life is not of a sexual nature. In a recent paper (6) I gave illustrations of what was supposed to "constitute life" amongst ordinary sensual individuals in bygone times, when the general public was, as a rule, little reticent on sexual matters, and did not endeavour so much as now to conceal the sexual factor in every-day life.

Then, as now, to the average kind of sensual individual, "life," or the sensual gratification of life, was largely a matter of (1) eating and drinking, satisfying to the full the imperious basic instincts of preventing starvation and thirst; of (2) hunting, sport, outdoor games and bathing, obtaining food and keeping one's body in health by suitable muscular exercise, cleanliness, and friendly competition; (3) indoor games, music, art, and social amusements, satisfying the instinct for ordinary pleasant domestic and social recreations and emotions. Sexual matters, that is to say, (4) functions and emotions connected with the instinct of reproduction, have always taken their due part in popular ideas of "life," though this is by no means such a large and exclusive part as some modern writers have apparently supposed.

We may safely take it, I think, that amongst ordinary sensual human beings of past and present times the basic and dominating desires and enjoyments of fully conscious (wakeful) life have been by no means limited to those of the sexual class—and so it is with dreams. The sexual element in dreams is doubtless greater than the sexual element in wakeful life, which is under conscious mental guidance; but sexual ideas, emotions, etc., do not by any means monopolise dreams. Ordinary individuals dream of ordinary incidents in their daily life, their ordinary occupations, duties, work, recreations, pleasures, successes, failures, disappointments, eating and drinking, riding, hunting, shooting, outdoor and indoor sports and games, music, art, and "hobbies," social entertainments, conversations with friends, etc. Naturally, in disordered states of the higher nervous system, due to shock, overstrain, fatigue, toxic

conditions, fevers, etc., and, when the stomach or intestines are distended or diseased, nightmare-like dreams of a terrifying nature are not uncommon. A neurotic child, brought up in an atmosphere of fairy tales of old-fashioned days, is likely often to dream of witches, hobgoblins, and man-eating ogres. A young woman saturated with the vampire legends of Eastern Europe, during the delirious stage of acute pneumonia, might have fancies resembling those of "Lenore" in G. A. Bürger's well-known ballad of that title (translated by Sir Walter Scott). So soldiers, during and after the dangers and strain of active warfare, may be restless and call out in their sleep, owing to exciting or terrifying dreams, as described by Lucretius and Shakespeare.

F. W. Mott, indeed, in his paper on the "Psychology of Soldiers' Dreams," (7) in which he gives the appropriate quotations from Lucretius and Shakespeare, has pointed out that fear, terror, and horror, connected as they are with the fundamental instinct of self-preservation, are at least just as likely to be represented in dreams as sexual ideas and emotions. The latter are connected with the important instinct of reproduction (propagation of one's kind and survival of the species), but the instinct of self-preservation is probably still more basic and still more dominating; both are, of course, especially powerful when the highest mental guidance is impaired, and when subconscious influences are allowed more or less uncontrolled play.

From whichever way one regards it, whether from the point of view of ordinary human experience or from that of theoretical probability, the Freudian teaching that nearly all dreams have a sexual explanation, is most unlikely to be true, or the element of truth in it is so exaggerated as to appear preposterous.

I do not believe that the elaborate Freudian explanation of dreams and morbid ideas by symbols is justified in the majority of cases by actual facts. Most persons do not usually think in symbols nor do they usually dream in symbols. But for those who seek a cryptic explanation on any subject, and by a kind of infatuation or self-suggestion believe that they have found one, no gulf in their line of argument is too broad to bridge over, no mouthful of improbability is too large to swallow, in order to convince themselves that they have proved the correctness of their arguments. Witness

the futile, though sometimes at first sight plausible, arguments and the wasted time (in searching for cryptographic clues, etc.) of those who set out to prove to others—after having almost convinced themselves—that the plays of Shakespeare were the work of Francis Bacon.[1] There are certain old Italian medals and plaques, cast in bronze during the sixteenth and seventeenth centuries, and perhaps later, which represent a fanciful profile portrait, so made that, on careful examination, it resolves itself into a number of *phalli*. The whole portrait (possibly originally devised as an "apotropæic" amulet for averting the "evil eye") is made up of these phallic emblems skilfully pieced together so as (all of them together) to represent the portrait in question. Several minor works of art, if they can be thus styled, of various periods are in existence in which either phalli or death's heads[2] or other symbols or emblems have been purposely concealed by the artist, who has evidently taken a delight in his skill in this direction. There have

[1] We have not yet heard the end of these discussions. If Shakespeare *could not* have written the plays, and if Bacon and other Englishmen *did not* write them, and if, after all, they were not "made in Germany," who, then, did write them? Why, it was Erasmus of Rotterdam, of course! He wrote them in Latin, one of them every night, during part of his visit to England, and gave them as a souvenir of his visit, to his friend, Sir Thomas More. When the latter was executed, the manuscripts passed, somehow or other, into the Bacon family, and, later on, Lord Bacon and Shakespeare made them topical and dished them up in English for the English court and the English people! No wonder that they contain echoes of the epigrams of Palladas and the Greek Anthology, that Erasmus so much admired! Oh, but what about the proof? The proof is a "cryptic" one, relying on cryptograms and symbols, but it is unfortunately not yet completely worked out!

[2] Here I might refer also to the hidden "death-mask" which it has been claimed was purposely included in the design of certain postage stamps issued in Serbia (1904) not long after the political murder of King Alexander I and his queen Draga (1903). The "death-mask" is said to resemble the features of the murdered sovereign. The stamps in question, commemorating the coronation of the royal successor, King Peter I, were engraved by Louis Eugène Mouchon, a Parisian artist well known in connection with the production of medals, plaques, postage stamps, etc. They became known as the "death-mask stamps," and the whole issue was quickly withdrawn by the Serbian government, but not before a great number had been circulated, and specimens can still be easily obtained from the dealers. The "death-mask" is seen only when the stamps are turned upside down. Harry de Windt ("Through Savage Europe," London, 1907, p. 164) alluded to the subject as follows: "Only a week after his arrival Peter sustained a severe shock in connection with the Jubilee stamp which was struck in commemoration of his coronation. The stamp bears the heads of the present ruler and his ancestor, 'Black George,' and at first sight the clever device of some revolutionary artist is unnoticeable. But turn it upside down and the gashed and ghastly features of the murdered King stand out with unmistakable clearness—just as they appeared when Alexander and his consort were discovered in the grey dawn of that summer's morning in the gardens of the old Konak. Needless to state, the issue was at once prohibited." My own opinion (F. P. W.) is that the presence of the so-called "death-mask" was a mere chance, though certainly a strange coincidence—a curious and undesired by-product of human art, analogous to a *lusus naturæ* or extraordinary effect produced in Nature's workshop, as when a pebble resembles a human head or a rock resembles a toad or a bird or a pulpit.

been collectors and archæologists, however, who have sought to find a *cryptic* phallus, or phallic signification, in most ancient (primitive) monuments and customs. Some of these investigators of origins may, indeed, have been said to have serpents and phallic emblems "on the brain." Similarly, some modern followers of Freud seem to have sexual explanations for almost everything, and sexual symbolism "on the brain."

The sexual instinct doubtless plays an immense part in the conscious and subconscious life of most individuals, but there are many other *driving motives in life* (8) besides those connected with sex, not to mention those very powerful ones—rivalry, resistance, and fear—connected as they are with the instinct of self-preservation. In the relatively primitive mental eyes of the ancient world, as I have already pointed out, "life was constituted," not merely by sexual enjoyments and emotions, but also doubtless (as now) by interesting occupations, professional work, ambitions and aspirations, eating, drinking, hunting, social amusements, games of various kinds, etc.

Is there any way of reconciling the Freudian teaching as to the sexual explanation of dreams (and human active life generally) with other considerations such as those I have alluded to? Yes! There is one, I think, namely, by arbitrarily altering the definition of such terms as "love," "libido," etc., so as to make "love" include almost every desire and passion, almost all psychical force, every thought or idea which activates life—in fact to make of it a kind of "joy of life," *élan vital*, a vital influence pervading everything, whatever human beings do or busy themselves about (*quicquid agunt homines*). This is, indeed, what, as it seems to me, Jung has done. Witness the following passages from his writings: (9) "All psychical phenomena can be considered as manifestations of energy in the same way as all physical phenomena are already understood as energic manifestations. . . . This energy is subjectively and psychologically conceived as desire. I call it *libido*. . . . From a broader standpoint *libido* can be understood as *vital energy in general*, or as Bergson's *élan vital*. . . . By *libido* I understand very much what Antiquity meant by the cosmogenic principle of *Eros*—in modern terminology simply *psychic energy*."

Truly all this is literally making "no end" of love; for according

to it everything is love, and it reminds me of the following motto or "posy" engraved on an old finger-ring:

"Like to this sirkell round
No end to love is found."

There is, I believe, a real element of truth in all this, in so far as (to a certain extent) superfluous sexual force may (by some process of metamorphosis, analogous to transformation of ordinary physical forces, according to the law of conservation of energy) be diverted into, and "activate" (?hormonic action) other and useful channels, so as to increase the quantity and quality of the physical and mental outputs in other directions. This consideration, by the way, likewise helps to explain some of the beneficial effects of work and occupation on the mind and body (10)—effects that have been admirably pointed out by Thomas Carlyle, in the enthusiastic encomium on work and labour included in his "Past and Present," which was published in 1843. Sir William Osler, in equally fine language, maintains the value of work in his Address to Students of Yale University (1913), in which he quotes Carlyle's sentence: "Our main business is not to see what lies dimly at a distance, but to do what lies clearly at hand." This does not mean, of course, that man should not live to some extent for the future. Most men derive pleasure from actively striving after results they hope to obtain in the future. The pleasure derived from hopeful endeavouring to obtain is often greater than the pleasure derived from actual possession. But I must leave off here before I am tempted to enter into another discussion which has little to do with my main subject.

POSTSCRIPT

In the above writing I have hesitated in describing the play of dream-like phantasies on going to sleep (including "hypnagogic hallucinations") as *quite* normal. Some persons of course are aware of none. Others, like myself, are aware of them at times, but not always, and their occurrence may be favoured by preceding mental excitement, or by mental stimulation, as for instance by tea, coffee, or certain toxic conditions connected with the alimentary canal. In my own case, it frequently happens that when sitting in the evening reading or studying I begin to doze: the scene changes, and

I hear various sounds, generally someone speaking to me or perhaps I hear myself addressing someone[3]—almost always on trivial, everyday, not disagreeable, subjects. For instance, someone may be asking me: "What time did you say," or "Have you left your gloves"—the scene varies; sometimes it may be the foot of a staircase very familiar to me. The associated general sensations are usually pleasurable and there is a feeling of *bien-être* (euphoria). Sometimes there is, however, an accompanying disagreeable oversensitiveness to *real* sounds (hyperacusis), as, for instance, when a person is actually talking in the same room, and there may be sensations of discomfort on being drawn back to ordinary wakeful life again.[4] Sometimes on commencing to doze, my thoughts remain (wandering) on what I have just been studying, and on waking up I find to my annoyance that I have only imagined myself to be still studying, and that in reality I have got no further on with my work (i.e., in reading a book) than when I commenced to doze. Sometimes, however, dozing or sleeping, after studying, has, as is well known, the effect of making problems of various kinds easier to solve, or of making one's work become less difficult to finish (the subconscious mind having adapted itself for that purpose during the interval of sleep).

[3] On these occasions I may have sufficient reasoning power left to conclude (from the memory of frequent previous experiences) that I am commencing to doze off over my work, and by a vigorous effort of the will I can sometimes shake the sleep off, get up from my chair, walk about, and then go on with my work again. I do not always identify the voices speaking to me with special individuals, though I feel that I could if I were to try. But this is true to nature in regard to myself, as the following occurrence shows. One night during the war I was walking home to Harley Street by Market Place, near Oxford Circus, thinking of something. There was little light owing to the danger of air-raids. Suddenly I felt a rather violent hand on my right shoulder and thought that some old friend of mine must be playfully disturbing my thoughts in that way. I did not trouble to look round, but the next moment a violent tug at my watch-chain roused me up. The watch-chain was gone (fortunately leaving the watch in my pocket) and a man was running away several yards in front of me. I gave chase and shouted "Stop thief" at the top of my voice. The chase was taken up by others, though I temporarily lost sight of the man. Someone was soon caught, who had many convictions to his credit in the police records, but he had not my watch-chain in his possession when he was caught, and, as the first thing I saw on this occasion was the back of a man running away, I could not swear that he was the man who seized my watch-chain. He was, therefore, discharged, somewhat to the annoyance of the special constable who had caught him. Strangely enough, several months later, the man in question, I think, whom I had seen in the dock, reappeared as a patient (though I did not at first recognise him). I took some blood from a vein to try the Wassermann reaction, but he did not like this and nearly fainted. and, to my annoyance, did not reappear at the hospital to hear the result and for further examination and treatment; he seemed also to have given a wrong address.

[4] It has occurred to me, as it doubtless has to very many others, that dying patients may sometimes feel anything but gratified on being temporarily dragged back to earthly life by hypodermic injections of strychnine, ether, and such like.

The "rapid play" of phantasies on commencing to "doze off" seems sometimes very remarkable and reminds me very much of what I have observed in patients with "busy" delirium tremens, only that my play of phantasies appears to me *kal*eidoscopic, whereas that of patients with delirium tremens is usually what might be termed *kak*eidoscopic.

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MYXEDEMA AND CRETINISM IN THE UNITED STATES AND CANADA: A STATISTICAL STUDY

By James M. Anders, M.D., LL.D., Philadelphia, Pa.

MYXEDEMA was first described by Sir William Gull (1) in 1873, although the name was suggested by William Ord (2) in 1877, while Charcot (3) in 1883 proposed that of "Cachexia pachydermique." Campbell Howard (4) has given an excellent summary of the steps in the development of our earliest knowledge of the subject. He has also detailed the histories of ten cases that occurred in the experience of Sir William Osler "either in private or in the wards of Johns Hopkins Hospital," and collected in addition ninety cases from accessible American and Canadian literature, prior to July 1, 1905.

One of the recognized effects of athyroidism or hypothyroidism is cretinism—a condition first described as a morbid entity by Curling (5) as early as 1850. The name sporadic cretinism, however, was first suggested by Hilton Fagge (6) in 1871, who expressed the prophetic view that "a waste of the thyroid might prove to be a constant character of the disease." Two additional varieties are recognized: endemic cretinism, of which no authentic examples have been recorded in America, and infantile myxedema, which may be included under sporadic cretinism for our purposes.

Osler (7) collected the cases of cretinism which had been recorded in the literature of the United States and Canada prior to 1893 and from other sources, and these formed the basis of an interesting and instructive paper presented to the American Congress of Physicians and Surgeons in May, 1893.

The reports of army medical examiners in the recent war have shown conclusively that organic developmental defects among the male adult population of the United States are widely prevalent. It may be assumed that in some cases at least these morbid deficiencies owe their origin to anomalies of structure and function of the ductless glandular system of early life.

This paper presents the results of a statistical investigation into the cases of myxedema that have been recorded in American and Canadian literature, together with authentic instances of the disease hitherto unreported from July 1, 1905, the date of the termination of Howard's collective inquiries, to July 1, 1918. In a similar manner and from the same sources the writer has presented the results of a review of the accessible literature on cretinism of these two countries, from 1893, when the statistical inquiries of Osler were terminated, to July 1, 1918.

With so-called mild myxedema caused by thyroid want—an interesting and important condition to which J. L. Reverden (8) first called attention 1886 and Hertoghe (9) has given much serious consideration—this paper cannot deal.

The recognition of this clinical variety of myxedema, however, is to be urged, since in ten cases observed by Moffitt (10) all manifested definite improvement under thyroid medication. The writer(11) has reported similar instances of the disease, and Pitfield has recorded a case of incomplete athyrosis successfully treated with thyroid extract.

Mention may be made of post-operative myxedema, which must be rare. The unavoidable inference, however, that total extirpation of the thyroid may cause a high degree of myxedema is amply confirmed by numerous experiments on animals. In response to a personal request addressed to a number of the leading American operators for hyperthyroidism, only 3 cases of undoubted operative myxedema were reported to me—2 by Plummer from the Mayo Clinic, and 1 by Ochsner, which followed the complete removal of the thyroid by Dr. Chas. T. Parkes in 1888, an operation at which he (Ochsner) assisted. These, added to the 4 recorded by Howard, make a total of 7 cases to date. The literature of Canada and the United States, strangely enough, contains no report of cases of this form of myxedema during the period covered by this statistical inquiry.

The pathogenesis of myxedema and cretinism has, in the main, long since been removed from the field of conjecture. Again, it is believed by some writers of note that the majority of the leading causes of the major pathological disturbances, e.g., syphilis, alcoholism, tuberculosis, and consanguinity, fall more or less heavily upon

the thyroid gland, and as the result the succeeding generation becomes the unfortunate inheritor of cretinoid subjects.

Edward T. Blake (12) long since pointed out that nutritional causes are involved in the production of goiter and cretinism, as confirmed by the fact that when semi-starvation was the ordinary state of things in country districts, these two diseases were endemic. In the light of this view it will become a matter of keen interest to note the effect of the recent great conflict of nations, with its ensuing deprivations and terrors of imminent starvation, on the incidence of both goiter and cretinism, more especially in Germany, Serbia, and the Balkans, where the pinch of lack of food was most severely felt. Doubtless the lessons of the war will confirm some of our preconceived notions, but it is not unlikely that they will also lay to rest some of our illusions.

Again, malnourished babes and young children are prone to develop certain affections in which the basal metabolism, as shown by Du Bois (13), is decidedly decreased, e.g., cretinism and hypothyroidism. Putnam investigated the histories of four cases of myxedema occurring before the twentieth year, and "in at least three of them, in spite of the scanty record of antecedents, there had been signs of degeneration, such as very low bodily weight; slight mental weakness; small, broad and depressed nose; and extremely broad tongue, indicating, perhaps, a partial and unrecognized cretinoid state since childhood." Pel (14) relates a case in point in which a syphilitic father had one son with myxedema and another with acromegaly. These remote etiological factors are of practical interest, bearing, as they do, upon the question of the treatment of the disease. It was on account of the traditional belief that athyroidism may be hereditary through the mother, or in some way indirectly the consequence of subnutrition dependent upon previous toxic degeneration of the thyroid, that an inquiry into the family history and other causative factors was included in the scope of the present investigations.

In order to be able to interpret the manifold symptoms of myxedema, it must be recollected that general infiltration of all the various systems of the body occur in this disease. A complete account of the diverse clinical features of myxedema is beyond the limits of the present discussion; they are so numerous and many so characteristic that individual recognition should not be difficult. Says

Dock (15): "Myxedema is easy to recognize if the symptoms are at all marked and the clinical picture borne in mind." It can, however, be safely stated that the professional conception of the disease is inadequate; this is particularly unfortunate, as myxedema is one of a few diseases for which we have a sovereign remedy.

On the other hand, a surprisingly small number of cases of myxedema have been recorded in American and Canadian literature during the last thirteen years, as is shown in the subjoined table, for the reason, in my view, that the condition is frequently overlooked. Indeed, so commonly has chronic nephritis been mistaken for this complaint outside of institutions in which careful, thorough examinations are systematically conducted, as to make fresh emphasis of the importance of its diagnosis highly desirable. Notwithstanding the fact that chronic Bright's disease and myxedema present few points of contact, clinically considered, but many of distinct dissimilarity, some of which are extremely striking, the latter is constantly and sadly being confused with the former disease.

One of the aims of the present investigations has been to indicate the effects of thyroid medication in these two conditions. True it is that in the case of myxedema there is unanimity of professional opinion as to the entire efficacy of thyroid extract, although the fact that complicating conditions, particularly in advanced cases, may present a contraindication to the use of this remedy in the usual dosage does not appear to be universally appreciated. For example, one of the cases belonging to my personal series presented marked cardiac dilatation and generalized arteriosclerosis with the usual accompanying urinary findings (small ring of albumen, long, narrow, hyaline tube casts), so that the beginning dose of thyroid was necessarily small and at no time could the customary dose of gr. 1-11 be administered without inducing toxic features. Here the fact that in some cases of myxedema, at least, a considerable portion of the gland may be structurally unaltered and capable of functioning, thus causing suspicion that the hypophysis or other endocrine organ may share in the causation of this disease, should be recollected. Again, Ponfick has pointed out that the hypophysis sometimes shows changes similar to those observed in the thyroid gland. Moreover, the thymus has been found to be enlarged in myxedema.

While rarely a mere functional loss of thyroid secretion is met with, e.g., in cases due to excessive child-bearing, shock, and the menopause, in many instances organic changes of an advanced character are presented by the gland at necropsy, including those peculiar to tuberculosis, syphilis, carcinoma, and endarteritis. These associated lesions assume importance in relation to both the treatment and prognosis.

Myxedema may follow local injuries, or an acute thyroiditis due to the acute infections, e.g., rheumatism, influenza, and erysipelas. In this group of cases life may be prolonged for an indefinite period under appropriate management.

Some of the newer points of view shed more or less light upon the problem of therapy in relation to both myxedema and cretinism. For example, Janney and Isaacson (16) have studied the partition of nitrogen in the urine both in hypothyroidism and after experimental hyperthyroidism, and have found that purin metabolism alone was altered, the output being decreased in hypothyroidism and increased in hyperthyroidism. No selective action on urea, ammonia, and creatinin was observed. The therapeutic action of thyroid, therefore, is attended with a gain rather than a loss of nitrogen; whereas loss of protein is due to the toxic action of the gland. According to this view an increased nitrogen output is an indication of over-dosage. Janney and Isaacson have further shown that following thyroidectomy in animals hypoglycemia results, and also a delayed blood sugar curve. Since the thyroid functions to maintain the normal blood sugar level, an intimate relation between this gland and carbohydrate metabolism most probably exists.

Janney (17) states that the typical exophthalmic goiter contains only from one-fifteenth to one-twentieth of the total active iodine present in normal thyroid; whereas more, not less, iodine might reasonably be expected to occur in hyperfunctioning glands. He further points out that similar metabolic disturbances may be present in both hyperthyroid and hypothyroid states, and that the blood picture in exophthalmic goiter is practically identical with that of myxedema, as evidence opposing the generally accepted view that these conditions are diametrically opposed. Janney has proposed the substitution of the term "dysfunction" of the thyroid gland for the obviously inadequate hyperthyroid explanation.

The *Journal of the American Medical Association* (18) comments editorially:

"In the light of this, we can now understand some of the symptoms of exophthalmic goiter—the thyroid enlargement, cutaneous symptoms, scleroma, osseous changes, and special metabolic manifestations, such as hypoglycemia—are identical with those of a hypothyroidism attributable to a poorly functioning gland. They are truly symptoms of thyroid deficiency which have usually been disregarded in the symptomatology. The more familiar manifestations—psychic stimulation, tremor, tachycardia, increased basal metabolism, etc.—are toxic symptoms which Janney assigns to the liberation of intermediate products of poisonous nature, perhaps owing to the incapacity of the glands to produce the normal thyroid hormine. In exophthalmic goiter, then, a toxic substance is circulating in the system. With a defective endocrine secretory function postulated, it becomes evident how hypothyroid and toxic symptoms may be discovered concomitantly."

It has not been my purpose to include the cases of exophthalmic goiter with marked deficiency symptoms in my series, but from personal observation and experience, I feel that in connection with their treatment the value of small doses, e.g., grs. ½ t.i.d. of thyroid extract, needs emphasis. On the other hand, larger doses would tend to induce toxic symptoms. Brooks and others have directed attention to the appearance of numerous cases of hyperthyroidism among soldiers in the recent world conflict. In some of these subjects certain clinical criteria of thyroid deficiency have also been present, according to their descriptions, and in such appropriate thyroid therapy was indicated. Bertine (19) notes the reports of recent cases in which hyperthyroid and hypothyroid symptoms were combined in the same person. Thanks to these investigations we are now enabled to direct the therapy of thyroid affections along more rational lines than in the past. Despite the recent important advances in our knowledge of the principal endocrine organs, however, we are far from being in a position to stabilize the balance of their interactivities.

Table I contains an epitome of the total number of cases of myxedema discoverable since July 1, 1905, the date of the termination of Howard's investigations, fifty-five in number, and these have been gleaned as before stated from three main sources, to wit, American and Canadian literature, 178 institutions, and leading individual physicians. To these are appended seven cases that have come under personal observation.

A brief statistical analysis of the figures and facts to be found in the table will not only prove valuable for comparison with other series previously published, but will also be an aid to the intelligent understanding of the results of our collective investigations.

Nationality. In 28 out of the 55 cases, 22 were American-born and 6 foreign-born, the latter being made up of English, Irish, and Russian, 2 each. As no mention was made of nationality in the remaining 27 cases, it may be inferred that the majority were Americans. The disease is rare in Germany and France, so that the absence of any cases from these countries need excite no surprise. The results of these inquiries throw but little light upon the distribution of the disease in the United States, although in general they show that its incidence is greater in the Northeastern sections, a statement confirmed by the recorded observations of previous writers. Moffitt, however, states that he believes the disease to be more prevalent in California than many other States, having collected 83 cases in that State alone.

Race. Few cases occur outside the white race, and certain writers have expressed the view that the negro is exempt. In my series two apparently authentic cases in the negro are included. Howard's series yielded only 1 per cent in the colored race, whereas my own gives an incidence of 3.7 per cent.

Age. The ages of my series range from twenty-one to sixty-nine years, which represent the extremes, while the average age for all in which it was noted was forty-five years. The average age for the females was forty-five years, while that of the males was thirty-nine years. These findings confirm those of Howard, who found that the disease is "relatively more common in the female from thirty to sixty and in the male from thirty to fifty."

In 26 cases both the age of the patient and duration of the disease were definitely given, and a simple computation shows that the average age of the period of development of the disease is eight and one-half years, or nearly a decade earlier in life than the above figure (forty-five) would indicate, or thirty-six and one-half years.

Sex. Sex has a potent effect on the incidence of the disease, females being the more frequent sufferers. In Howard's 100 cases the ratio of 6.6 to 1 obtained, while in my own, consisting of 54 in which the sex was recorded, 45 were females and 9 males (5 to 1). These two series were drawn solely from the United States and Canada.

Heredity. The results obtained in the present inquiry confirm the opinion that heredity plays a not potent, but definite etiological rôle. For

TABLE I

AUTHOR	REFERENCE	NATIVITY	AGE	SEX	HEREDITY	OTHER ETIOLOGICAL FACTORS	COMPLICATIONS	UNRECOGNIZED	DURATION	EFFECTS OF TREATMENT
M. W. Dvorak.	*Wisconsin M. J.*, 1909-10, viii, 575.	—	32	Female.	—	—	Pruritis vulvæ.	—	—	Symptomless during treatment.
W. B. Thistle.	*Can. Pract. & Rev.*, Toronto, 1910, xxxv, 357.	—	56	Female.	—	Had had several miscarriages; severe hemorrhage with last.	—	Yes (pernicious anemia).	About 4 years.	Much improved by treatment. Still under treatment.
G. S. Derby.	*J. Am. M. Assn.*, Sept. 21, 1912, 1045.	—	56	Female.	Negative.	Arsenical poisoning a few years previously.	Slight edema of feet, slight trace of albumin, eye manifestations.	—	—	Marked improvement.
G. S. Derby.	*J. Am. M. Assn.*, Sept. 21, 1912, 1045.	—	49	Male.	Negative.	Kicked in face 15 and 13 years ago.	Albumin and sugar present, eye manifestations.	—	—	—
F. M. Horsley.	*Virginia M. Semi-Month.*, Oct. 11, 1912, 332.	American Negro.	—	Female.	—	—	Impaired vision, coma and convulsions. No albuminuria. Sugar present once.	—	—	Kept in quite good health on thyroid treatment.
J. H. Pratt.	Not reported.	—	51	Female.	Negative.	None.	Albumin, casts and "edema."	Yes.	2 years.	Cured.
E. A. Christian.	Not published	—	57	Female.	None.	Pregnancy and childbirth.	Mental symptoms chiefly weakness with amnesia.	—	29 years.	Cured.
G. E. Charlton.	Not published.	American.	31	Female.	—	—	Insanity.	—	6 years.	—
A. E. Roussel.	Not published.	Russian Hebrew.	50	Female.	Tuberculosis in collateral branches.	Menopause irregularities.	Albuminuria.	Yes. (Bright's).	Some years.	Practically cured of myxedema. Died suddenly—autopsy—myocarditis.
A. E. Roussel.	Not published.	Russian Hebrew.	38	Female.	Negative.	Pregnancy and fright.	Slight albuminuria.	Yes (Bright's).	2½ years.	Prompt cure.
R. M. Elliott.	Not published.	American.	59	Female.	Negative.	—	Dwarf, imbecile, slight enlargement of thyroid.	—	—	—
Owen Copp.	Not published.	American.	21	Female.	Negative.	Negative.	Committed suicide.	—	—	Did not improve.
Owen Copp.	Not published.	American.	58	Female.	Father alcoholic.	Mother and sister erratic.	Extreme mental and physical apathy.	Previously recognized.	—	Improved rapidly on thyroid treatment.
H. I. Klopp.	Not published.	American.	61	Female.	Negative.	Negative.	Auditory and visual hallucinations—anemic.	—	—	Recovered on 2-grain tablets at night, then increasing dosage.

TABLE I—*Continued*

AUTHOR	REFERENCE	NATIVITY	AGE	SEX	HEREDITY	OTHER ETIOLOGICAL FACTORS	COMPLICATIONS	UNRECOGNIZED	DURATION	EFFECT OF TREATMENT
G. Loop.	*N. Y. State J. M.*, Oct., 1905, p. 373.	—	—	Male.	Paternal cousin had simple goiter.	—	—	—	—	Almost total disappearance of symptoms ten weeks after admission.
G. Campbell, Jr.	*Quart. Bull. M. Dep. Wash. Un.*, 1906–7, v. 50.	—	48	Female.	Neurotic.	—	Dropsy of legs due to weakness.	—	—	Cured.
G. Campbell, Jr.	*Quart. Bull. M. Dep. Wash. Un.*, 1906–7, v, 50.	—	47	Female.	—	—	—	—	—	Improving.
F. G. Finley.	*Montreal M. J.*, 1905, xxxiv, 890.	—	—	Male.	—	—	—	—	—	Cured.
L. J. Harvey.	*Med. Fortnightly*, St. Louis, 1905, xxviii, 597.	—	52	Female.	—	—	—	—	—	Cured.
L. E. Hertzler.	*Am. J. M. Sc.*, Feb., 1906, 245.	—	44	Male.	—	—	No albumin or sugar ascites.	—	—	Cured.
Chas. Stover.	*N. Y. State J. M.*, Dec., 1907, 477.	—	Post climacteric.	Female.		—	Ascites and edema. No albumin.	—	—	Cured.
J. B. Marvin.	*Louisville Month. J. M. & S.*, 1908–9, xv, 188.	—	—	Male.	—	—	—	—	—	—
J. B. Marvin.	*Louisville Month. J. M. & S.*, 1908–9, xv, 188.	American Negro.	"Young woman."	Female.	—	—	—	—	—	Now an imbecile; treatment not mentioned.
J. N. Sloan.	*Centr. States M. Monit.*, Ind., 1908, xi, 49.	—	36	Female.	—	—	—	—	—	Cured.
J. W. Lee.	*Kentucky M. J.*, Aug., 1908, 418.	—	51	Female.	—	—	Uterine hemorrhage.	—	—	Improving.
S. MacCuen Smith.	*Laryngoscope*, 1910, xx, 545.	—	—	—	—	—	Aural symptoms.	Yes.	—	—
S. MacCuen Smith.	*Laryngoscope*, 1910, xx, 545.	—	52	Female.	—	—	Aural symptoms and bleeding from nose and mouth.	—	—	Cured.
S. MacCuen Smith.	*Laryngoscope*, 1910, xx, 545.	—	56	Female.	—	—	Aural symptoms.	—	—	Cured.
R. L. Pitfield.	*Am. J. M. Sc.*, July, 1909, 92.	American.	40	Female.	—	—	Carcinoma of breast, uterine hemorrhage; albumin and casts.	—	—	Wonderfully improved

R. L. Pitfield.	*Am. J. M. Sc.*, July, 1909, 92.	—	62	Female.	—	Menopause.	True edema due to weak heart; joint pains.	—	15 years.	Cured by 2-grain doses t. i. d. Lost 24 lbs. in one month.
R. L. Pitfield.	Not recorded.	Irish.	45	Female.	Negative.	Followed double oophorectomy.	Albuminuria and decompensated heart with anginal symptoms.	Yes.	10 years.	Moderately good; requires small doses constantly.
R. L. Pitfield.	*Am. J. M. Sc.*, Dec., 1907, 859.	English.	45	Female.	Negative.	13 children in quick succession.	Cardiac weakness. Tremor.	No.	5 years.	Cure after 18 months' treatment (gr. 15 to 30 daily).
R. L. Pitfield.	*Am. J. M. Sc.*, Mar., 1916, 409.	"von L."	Late 30's	Female.	—	—	Profuse hemorrhages from uterus. Movable kidney. Tinnitus aurium. Marked mental depression. Slight edema of legs. Cardiac decompensation.	No.	5 years.	Cured.
R. L. Pitfield.	*Am. J. M. Sc.*, Mar., 1916, 409.	Irish.	41	Female.	Negative.	Scarlatina, 4 children.	Edema of legs due to cardiac weakness. Hallucinations. Tinnitus aurium. Paraesthesia. Trace of albumin.	No.	9 years.	Cured.
R. L. Pitfield.	*Am. J. M. Sc.*, Mar., 1916, 409.	—	46	Female.	Psychopathic tendencies.	Scarlatina, 11 children rapidly, 2 abortions.	Uterine hemorrhages. Mental aberration.	No.	5 years.	Cured.
R. L. Pitfield.	*Am. J. M. Sc.*, Mar., 1916, 409.	—	53	Female.	Negative.	4 children.	Profuse uterine hemorrhages at menopause. Casts and albumin in urine. Legs edematous. Tremor in hands —hypertension— motor aphasia.	No.	—	Heart depressed at first.
S. E. Simmons.	*J. Am. M. Assn.*, lii.	American.	36	Male.	Negative.	—	—	—	24 years.	Cured in 5 weeks under 2-grain doses.
W. D. Reid.	*Boston M. & S. J.*, clxxii, No. 18.	American.	69	Female.	Sister had thyroid disease. Takes thyroid extract regularly.	—	Slight possible trace of albumin.	Yes (thought to be chronic nephritis)	years.	Death due to bronchopneumonia. Markedly improved as to myxedema.
E. F. Leonard.	*Med. Rec.*, xxviii, 1914.	American.	32	Male.	Negative.	Alcoholism on father's side and severe shock from suicide of brother-in-law.	Insanity, delusions, hallucinations.	Yes.	5 years.	Cured; takes gr. ii daily.

TABLE I—*Continued*

AUTHOR	REFERENCE	NATIVITY	AGE	SEX	HEREDITY	OTHER ETIOLOGICAL FACTORS	COMPLICATIONS	UNRECOGNIZED	DURATION	EFFECT OF TREATMENT
W. T. Watson.	*Maryland M. J.*, lviii, 39.	American.	64	Female.	Negative.	—	Delusions of cats, rats and dogs in house.	Yes (chronic nephritis).	3 years.	Cured; requires gr. ii daily.
E. N. Brush and W. B. Cornell.	*Arch. Int. Med.*, 1912, xi, 530.	—	41	Female.	Negative.	—	Faint trace albumin.	Yes (Bright's and tumor base of brain).	5 years.	Symptomless for seven years under treatment.
J. E. Perrung.	*Lancet-Clinic*, Cincin., May 22, 1915, 584.	—	17	Female.	Negative.	—	Mentality of 2 years ("congenital deficiency or absence of thyroid").	—	—	Much improved.
M. B. Heyman.	Not published.	—	35	Female.	Negative.	One sister nervous.	Two severe uterine hemorrhages.	—	3 years. (3)	Slight improvement in general condition. Dose of thyroid not stated.
P. G. Taddiken.	Not published.	American.	45	Female.	Negative.	Negative.	None.	Yes, on two occasions.	—	Noticeable improvement on small doses of thyroid, skin becoming normal.
S. Solis Cohen.	Not published.	—	26	Female.	Negative.	Said to have followed grippe 3 years ago.	—	No.	3 years.	—
W. Harmer Good.	Not published.	American.	43	Male.	Negative.	Followed acute illness resembling grippe.	Pituitary disease. Testicular atrophy. Died of pneumonia. Thyroid greatly atrophied at autopsy. Had intercurrent febrile attacks. Persistent thymus tissue.	Yes, until seen by Dr. Good.	17 years.	Lost all myxedematous symptoms on gr. iii thyroid daily.
W. Harmer Good.	Not published.	American.	38	Female.	Father an alcoholic.	Was assaulted by burglar about 2 years previously.	Albuminuric retinitis; few tube casts; no albuminuria.	Yes, until seen by Dr. Good.	8 years.	Cleared up but could not take gr. i t. i. d. without inducing palpitation. Retinal changes and casts did not disappear.
W. Harmer Good.	Not published.	American.	26	Female.	Father an alcoholic.	Five children born in rapid succession.	None except "marked mental depression."	Yes, until seen by Dr. Good.	7 years.	Recovered on gr. iii daily. Not maximum dose.

J. M. Anders.	Not published.	American.	48	Female.	Negative.	None.	Menopause — albuminuria and few hyaline tube casts.	Yes (Bright's).	10 years.	Cure. Loss of 40 lbs. in 3 weeks; gr. ii–v t. i. d.
J. M. Anders.	Not published.	American.	21	Male.	Addison's disease; tuberculosis marked.	None.	"Edema of ankles and eyelids."	Yes.	3 years.	Cured.
J. M. Anders.	Not published.	American.	34	Female.	Negative.	Frequent tonsillitis during adolescence. Tuberculosis of tubes and ovary—operation.	Amenorrhea for 10 years. *Associated acromegaly.* Marked anemia.	Yes.	10 years.	Definite improvement from combined use of thyroid and pituitary extracts, āā gr. ½ t. i. d.
J. M. Anders.	Not published.	American.	53	Female.	Negative.	Removal of both ovaries 12 years previously.	—	Yes.	18 mos.	Cured.
J. M. Anders.	Not published.	American.	35	Female.	Tuberculosis on mother's side.	One miscarriage followed childbirth. Rheumatism as child. Tonsillitis at 27.	None, except slight albuminuria for 5 years.	Yes, diagnosed as chronic nephritis.	5 years.	Thyroid extract gr. i. Cured. Disappearance of myxedematous symptoms including albuminuria.
J. M. Anders.	Not published.	American.	58	Male.	Negative.	Grippe just before onset.	None.	No.	15 years.	Recovered.
J. M. Anders.	Not published.	English.	—	Female.	Negative.	None.	Albuminuria, casts, marked anemia and cardiac decompensation.	Yes (Bright's).	18 mos.	Marked improvement. Could take only gr. ½ of thyroid extract t. i. d.

example, in the case reported by Reid one sister most probably suffered from thyroid deficiency (see table), while in that of Loop a paternal cousin had simple goiter. In one case the family exhibited "psychopathic," another "neurotic," and in still another "erratic" tendencies. It would appear obvious that family neuroses are to be included among the predisposing causes. The table gives 3 case reports in which there was a family history of tuberculosis (5.4 per cent). This percentage is much smaller than that given by certain other observers, e.g., Hun and Prudden found phthisis in the near relatives in 9 (17 per cent), Howard in 10 (14.7 per cent), the London Committee 20 (28 per cent). Of my own cases recorded in the table, 7 in number, 2 (28.5 per cent), it will be observed, gave a history of tuberculous antecedents. In view of these facts it is clear that tuberculosis exerts a predisposing influence of moderate degree in the causation of myxedema. As to syphilis as an hereditary factor my table is peculiarly silent. Other observers, including Hun and Prudden and Howard, have found a few examples of this disease among the antecedents of myxedema patients.

In my series of 55 cases are 3, or 5.5 per cent, in which alcoholism in the father was noted, while in Howard's American series of 100 cases only 2, or 2 per cent, gave a history of alcohol. Statistical evidence to show that alcoholism and syphilis play an important rôle as causative factors, as has been claimed, is here wanting.

Other Etiological Factors. Among etiological and pathogenetical factors certain acute infections would appear to occupy an inconspicuous place. Of my series of 55 cases, the disease followed an attack of "grippe" in 3 instances, scarlatina early in life in 2, acute tonsillitis in 2, one of the latter also having had acute rheumatism as a child. The etiological relation of rheumatism to thyropathic states is generally recognized, more particularly to exophthalmic goiter. It is worthy of note that myxedema apparently followed influenza immediately in at least 2, and most probably 3 cases, of my series, and it would seem unlikely that the association was purely accidental. There is no evidence of acute thyroiditis in these cases, and it is not improbable that they are primarily instances of toxemic shock. Chronic atrophy of the gland, which is so commonly found in athyroidism, has its origin, in a few cases at least, in the above-mentioned acute infections, complicated with acute thyroiditis.

It would appear to be established that multipara are more prone to myxedema than single women and nullipara. This view is confirmed by my own statistical researches, as the table will show. For example, 1 of the series had thirteen children, 1 eleven children, 2 four children each, and 1 five (11.1 per cent). The influence of the marital state upon the incidence

of the disease is further shown by the history of miscarriages, preceding its development (see table). In some of the above cases mention was made of rapid childbearing, in 2 the condition appeared to date from "pregnancy and fright," and in 1 from "last child birth." Of the 46 cases in females, 6 had uterine hemorrhages, mostly profuse. In 4 females of my series, the complaint probably dated from the menopause. In only 3 of Hun and Prudden's cases and in 1 of Howard's series was it definitely stated that the disease commenced at the menopause. In 7 of Howard's cases, however, the menopause preceded the disease. "As myxedema is most frequent in women between the ages of forty-five and forty-nine, the usual ages for the menopause, atrophy of the thyroid and with it myxedema may have some fairly constant relation to changes in the menstrual function" (Howard).

In 2 cases observed by me anemia of the secondary type was well marked. This symptom has received emphasis from certain writers, but it is by no means constant. For example, Dock states that anemia is present in one-half of the cases. Again among recognized causative factors nervous shock has held a conspicuous place in the experience of clinicians.

Diagnosis. Out of 27 cases belonging to my series (see table) not less than 20, or 74 per cent, had gone unrecognized by one or more clinicians, including physicians of large caliber. Again, the average duration for these 27 cases was five years. This is a sorry commentary when it is recollected that, once recognized and the sovereign remedy employed, a cure is usually attained in three to five weeks. Admitting that it is difficult to determine the point at which the condition commences, failure to recognize a reasonably well-characterized case is inexcusable in view of the excellent delineation of the diagnostic features to be found in classic articles on the subject and in medical text books and systems of medicine. Efforts to stimulate interest in the subject, therefore, would appear to be sorely needed.

As intimated, in the majority of cases in which an erroneous diagnosis had been made, chronic nephritis had been mistaken for myxedema. Of the 7 cases in the table that have fallen under personal observation 4 had been diagnosticated chronic Bright's, owing to the presence of albuminuria, with or without tube casts, or the presence of edema. Of the total number of cases in which the complications were noted in the table, or 43, urinary features or such symptoms as would suggest chronic nephritis to the superficial observer, e.g., myxedematous infiltration of skin, were present in 18, or 41.8 per cent. But though albuminuria is here grouped with the complications noted (see table), it is in reality a common symptom, and if this fact were borne in mind fewer wrong diagnoses would be made. Edema was reported in 8 out of the 55 cases, or 14.5 per cent, and while this symptom may be an accompaniment of the complaint due to anemia, cardiac

decompensation, or actual nephritis, the error of mistaking the thickened skin of the face and legs of myxedema, which does not pit to pressure, for true edema, is all too common, and, moreover, has led men of high competence in the profession to make the diagnosis of chronic nephritis.

The column of the table that is devoted to treatment tells its own story so far as the effects of thyroid medication are concerned. The case of acromegaly with associated myxedematous infiltration of the skin received marked and prompt benefit from the combined use of pituitrin and thyroid extract. Putnam (20) has recorded 3 cases which stand close to both myxedema and acromegalia especially, the latter in 2 of them, and in all of which the use of thryoid gland was remarkably effective for good. It is noteworthy that the symptoms of cardiac origin during thyroid treatment, the tachycardia in particular, are due to the toxic action of this drug. The indications presented by complications, causative factors, and especially signs of malnutrition, must be met in accordance with accepted therapeutic principles.

From the above analysis, the principal interest and chief importance attaches to the following points revealed: (*a*) The remarkable percentage of cases in which the complaint is overlooked, and the frequency with which chronic nephritis and other morbid conditions are mistaken for myxedema; (*b*) the close relationship between myxedema and rapid childbearing, pregnancy, and the menopause; (*c*) the acute infections, particularly influenza, as points of origin of the condition; (*d*) the not very uncommon association with myxedema of disturbances of endocrine organs other than the thyroid, e.g., Addison's disease in one, and pituitary lesions in my two cases; (*e*) the specificity of thyroid medication and the necessity for employing this agent in small doses, so as to avoid toxic effects; and (*f*) the practical importance of directing measures to any complications present and near and remote etiological influences in the individual cases.

Cretinism. The belief that cretinism is common in severe goiter districts of Europe is not borne out by the reports coming from institutions in the regions in which goiter is most prevalent in this country. It must, however, be admitted that allowances are to be made in a statistical study of the disease for omissions on this point and for errors of diagnosis.

Osler's inquiry as to the prevalence of sporadic cretinism in this country (*supra*) revealed, to quote his words, that "much

misunderstanding exists as to the exact definition of a cretin illustrated by the fact that at least one-half of the photographs sent me from different institutions did not belong to this type of idiocy." He continues: "The term should be limited accurately to a form of idiocy associated with changes in or absence of the thyroid gland." The condition may be of embryologic origin, in which there is a nondevelopment or partial development of the thyroid gland. In sporadic cretinism the gland is usually absent or greatly atrophied, although mention of this fact is rarely made by writers in their reports of cases. This variety usually arises during childhood following some serious illness. In the endemic form "the thyroid gland is very commonly enlarged, but in all probability functionless" (Osler). It has been observed that when people migrate into a goitrous district this disease is likely "to show itself in the first generation, cretinism in later ones" (Dock). The present collective inquiry lends color to the significance of this statement, although it was not particularly devoted to this phase of the subject. While the etiological identity of myxedema and cretinism is pretty generally recognized, Buschan and Bircher oppose the view. Dock (21) affirms that "since removal of a goitrous thyroid from a cretin may be followed by myxedema, cretinism may be looked upon as an incomplete myxedema."

The fact that cretinism is less susceptible of improvement from thyroid medication than myxedema, a view confirmed by the present investigations, would seem to indicate that additional factors must enter into one's conception of the causation of the former condition. For example, specific treatment may fail to effect definite improvement, particularly in the mental faculties, of the cretin. Here it should be recollected that the younger the cretin the more pronounced the degree of idiocy. Ewald's statement concerning myxedema, i.e., "Notwithstanding the remarkable results obtained with thyroid extract in this complaint, something yet seems to be needed to bring back absolute mental activity and well being in these cases," is far more strikingly true of cretinism.

Again, Paschoud's view that no benefit is derived from thyroid grafts in cretinism is to be mentioned, as indicating the possibility of the operation of extraneous causative factors, by comparison with myxedema. Further examination of endocrine disease may possibly

consign cretinism to the indefinite group spoken of as polyglandular affections. In this connection the results of the experiments of Kendall (22) are pertinent and significant. These furnish convincing evidence that "thyroid activity in the absence of a simultaneous suprarenal cortex activity does not produce the usual hyperthyroid symptoms, but instead, a depression." In other words, the suprarenal cortex activity must convert the ammonia into a pre-urea compound, or otherwise a high protein intake, hyperactivity of the thyroid notwithstanding, will induce depression. For the present, however, rigid adherence to the athyroid origin of cretinism is advisable, so that the use of our sole promising remedy may not fall into professional disrepute. From these investigations it is also clear that, even at the present day, confusion of this complaint with pathologically unrelated forms of idiocy and dwarfism is not rare, a fact that may in a measure at least explain the less prompt efficacy of, and sometimes distinctly unsatisfactory results from, thyroid preparations.

According to Janney's studies the depression of metabolism, which has long been recognized in cretinism, cannot be due to intestinal stasis, with its decreased alimentary absorption of food. The adiposity sometimes observed, however, may be accounted for by an altered assimilation of sugar, since disturbances of carbohydrate metabolism have now been demonstrated to attend hypothyroid conditions. As above pointed out, Du Bois has shown that in cretinism the basal metabolic rate is decreased. While, therefore, the precise function of the so-called endocrine glands is unknown, there can be no longer any doubt that several of them, e.g., the thyroid, the pituitary, and adrenals, each play an important rôle in basal metabolism.

The diagnosis of typical and advanced cases is free from difficulty. Koplik has reported a case in a child aged one month, and pointed out that even in very young patients the characteristic features are present. Recognition of the disease is based on the peculiar physical characteristics, mental condition, and changes that occur in the skin, as well as other features so clearly set forth by Osler (23), who also describes three grades of the affection. Osler quotes Horsley, whose words, he tells us, form the basis of the classification:

"By excluding all cases in which the appearance of idiocy is not accompanied by any noteworthy changes in the skin or connective tissues, we obtain a considerable delimitation of the condition which we ought to call cretinism, for by adopting such a plan of differentiation we necessarily leave out all cases due to direct injury or disease of the central nervous system, and which are included in the conditions classed by various writers under different headings, such as congenital idiocy, idiocy following encephalitis, idiocy coupled with parencephaly, etc., all being cases where we have destructive lesions or non-development of the central nervous system, especially of the cerebral hemispheres, and in which, therefore, we have a simple and direct destruction of the intellectual mechanism. Although such conditions may be naturally accompanied by want of development in the parts of the body which may happen to be paralyzed, etc., still there is no direct or certainly no general change in the connective tissues throughout the whole system, and secondarily in the nervous system, such as furnishes the basis of the present classification."

Osler made inquiries which related to sporadic cretinism only, of which he could find but 3 cases recorded in the literature of this country up to date (1893). To these should be added 3 additional cases, which appeared in rapid succession at the Johns Hopkins Hospital in his wards, and 8 well-characterized examples, the result of letters sent out to all of the Asylum Superintendents in the United States and Canada and to various institutions for feeble-minded and idiotic children for information as to the existence of the disease. Of the latter 8 and his own 3 hospital cases, Osler gives an interesting detailed description.

My own inquiries were addressed to practically identical sources, to wit: American and Canadian literature, representative physicians, and institutions for feeble-minded as well as orphan asylums and hospitals for the insane. The literature yielded 28 cases, while from the other sources there were 45, making a total of 73 cases, as shown by Table II. The points covered in the individual examples of the disease are indicated at the head of the different columns.

Incidence. While according to the tables the total number of cases of myxedema was only 55 and that of cretinism 73, it is to be recalled that the period covered by these collective investigations was only thirteen years for the former and twenty-five years for the latter condition. Hence the incidence would appear to be greater for myxedema than for cretinism.

TABLE II

AUTHOR	REFERENCE	NATIVITY	AGE	SEX	CONDITION OF THYROID	HEREDITY	OTHER ETIOLOGICAL FACTORS	COMPLICATIONS	UNRECOGNIZED	DURATION	EFFECT OF TREATMENT
H. Heiman.	*Arch. Pediat.*, 1905, xxii, p. 846.	—	17 mos.	Female.	—	Negative.	Pertussis at 6 mos. of age.	—	No.	10 mos.	Marked improvement.
E. G. Randall.	*Hahneman. Month.* 1905, xl, p. 683.	—	12 yrs.	Female.	Not palpable.	Negative.	Cold on lungs at 8 mos. of age.	Inguinal hernia.	Yes by 7 or 8 Doctors.	12 yrs.	Perceptible improvement at end of 2 weeks, marked in 6 months.
J. C. West.	*Arch. Pediat.*, N. Y., p. 1906, xxiii, 603.	—	10 yrs.	Female.	—	Negative.	None.	None.	Yes by several.	15 mos.	Marked improvement of mind and appearance.
F. L. Vonsickle.	*Tr. Lackawanna Co. M. Soc.*, Scranton, 1905, i, p. 134.	American.	6 yrs.	Female.	—	Negative.	Fall at 10 mos., pertussis at 14 mos., inflammation of bowels at 26 mos.	Cervical glands enlarged.	No.	3 yrs.	Marked improvement.
E. S. Everhard.	*J. Am. M. Assn.*, 1906, xliii, p. 205.	American.	12 yrs.	Female.	Very small.	Father had chronic nephritis.	Sister never strong, one brother had asthma, another very nervous.	Acute indigestion.	Yes.	10 yrs.	Marked improvement from treatment and spontaneous establishment of menstruation.
R. W. Soper.	*J. Am. M. Assn.*, 1907, xlix, p. 1674.	American.	8½ yrs.	Female.	—	—	None.	None.	Yes by several.	8½ yrs.	Marked improvement after 4 months' treatment.
L. S. Monson.	*Med. Rec.*, N. Y., 1910, xxvii, p. 7.	American, twin.	24 yrs.	Male.	Small.	Negative.	None.	Petit and grand mal.	Yes.	—	Not so marked as brother.
L. S. Monson.	*Med. Rec.*, N. Y., 1910, lxxvii, p. 7.	American, twin.	24 yrs.	Male.	Small.	Negative.	None.	Ataxia.	Yes.	—	Marked improvement.
W. B. Hoag.	*Med. Rec*, N. Y., 1910, lxxvii, p. 857.	American.	6 mos.	Male.	—	Negative.	Possible trauma at birth.	None.	No.	6 mos.	Slow and gradual improvement.
Etta Charles.	*J. Indiana Med. Assn.*, 1909, ii, p. 470.	American.	14 yrs.	Female.	—	Father died drunkard and mother of tuberculosis.	None.	—	—	14 yrs.	Marked improvement.
J. E. Show.	*Kansas City M. Index-Lancet*, 1909, xxxii, p. 352.	American.	2½ yrs.	Male.	—	Negative.	Normal baby till 2 years of age.	None.	No.	6 mos.	Wonderful improvement.
N. L. Niles.	*Providence M. J.*, 1910, xi, p. 154.	American.	6½ yrs.	Female.	—	Negative.	Scarlet fever, pertussis and cholera infantum.	None.	Yes.	4½ yrs.	Marked improvement.

N. L. Niles.	*Providence M. J.*, 1910, xi, p. 154.	American.	5 yrs.	Male.	—	Negative.	None.	None.	—	4 yrs.	Marked.
N. L. Niles.	*Providence M. J.*, 1910, xi, p. 154.	American.	6 yrs.	Male.	—	Negative.	Instrumental delivery, sunstroke.	None.	—	5 yrs.	Marked.
J. B. Nowlin.	*Old Dominion J. of M. & S.*, 1908, vii, p. 408.	American.	23 mos.	Male.	—	Negative.	None.	None.	—	19 mos.	Very noticeable.
Geo. E. Price.	*Am. Med.*, Burlington, Vt., and N. Y., 1911, vii, p. 407.	American.	14 yrs.	Male.	—	Negative.	Blue baby.	None.	No.	14 yrs.	Marked improvement.
Maude Glasgow.	*Woman's M. J.*, Cincin., 1912, xxii, p. 199.	American.	12 yrs.	Female.	—	Negative.	—	None.	Yes.	7 yrs.	Marked improvement.
B. B. Brim.	*Toledo M. & S. Reporter*, 1910, xxxvi, p. 563.	American.	17 yrs.	Male.	—	Mother developed a goiter 2 or 3 years before his birth.	None.	Rheumatism, cardiac and Bright's disease.	—	17 yrs.	No treatment mentioned.
B. B. Brim.	*Toledo M. & S. Reporter*, 1910, xxxvi, p. 563.	American.	18 yrs.	Female.	—	Mother developed asthma 3 years before her birth.	None.	None.	No.	18 yrs.	Marked improvement.
W. H. Ross.	*Long Island M. J.*, Brooklyn, 1912, vii, p. 121.	American.	18 mos.	—	—	Negative.	None.	None.	No.	18 mos.	Marked improvement.
F. L. Stone.	*West. M. Rev.*, Omaha, 1913, xviii, p. 201.	American.	8 mos.	Female.	—	One cretin on father's side.	—	None.	-	8 mos.	Rapid improvement.
A. C. Kimball.	*J. Cutan. Dis. incl. Syph.*, N. Y., 1913, xxxi, p. 271.	American.	5 yrs.	Male.	Unpalpable.	Mother had goiter, also two of mother's sisters.	—	None.	—	5 yrs.	Not stated.
A. L. Breier.	*Wisconsin M. J.*, Milwaukee, 1915–1916, xiv, p 15.	American.	14 yrs.	Male.	Unpalpable.	Father died from paralysis.	None.	None.	—	13 yrs.	Improvement.
A. L. Breier.	*Wisconsin M. J.*, Milwaukee, 1915–1916, xiv, p. 22.	American.	19 yrs.	Female.	Unpalpable.	Negative	None.	None.	—	19 yrs.	Improvement.
G. M. Williamson.	*Journal-Lancet*, Minneap., 1914, xxxiv, p. 501.	American.	5½ yrs.	Female.	—	Negative.	None.	None.	—	3½ yrs.	Rapid improvement.
F. B. Talbot.	*Am. Dis. Child.* Chicago, 1916, xii, p. 145.	American.	3 yrs. 8 mos.	Male.	—	Negative.	None.	None.	—	3 yrs. 8 mos.	Marked improvement.

TABLE II—*Continued*

AUTHOR	REFERENCE	NATIVITY	AGE	SEX	CONDITION OF THYROID	HEREDITY	OTHER ETIOLOGICAL FACTORS	COMPLICATIONS	UNRECOGNIZED	DURATION	EFFECT OF TREATMENT
W. B. Hoag.	*Med. Rec.*, N. Y., 1916, lxxxix, p. 755.	—	5½ yrs.	Female.	—	—	None.	None.	No.	5 yrs.	Practically a cure.
W. H. Edelman.	*Arch. Pediat.*, N. Y., 1916, xxxiii, p. 932.	American.	3½ yrs.	Male.	—	Negative.	None.	Eczema.	Yes.	3½ yrs.	Marked improvement.
Wm. J. Stewart.	Not published.	American.	10 yrs.	Female.	—	Brother a cretin. Uncle tuberculous. Aunt has goiter.	Negative.	None.	No.	10 yrs.	—
Wm. J. Stewart.	Not published.	American.	12 yrs.	Male.	—	Sister a cretin. Uncle tuberculous. Aunt has goiter. Grandfather alcoholic. Epilepsy and feeble-minded among remote ancestors.	Negative.	None.	No.	12 yrs.	Thyroid treatment did not result in any marked improvement.
Wm. J. Stewart.	Not published.	Italian.	18 yrs.	Female.	—	Mother immoral. Maternal grandfather alcoholic. Brother mentally deficient.	Negative.	None.	No.	About 15 yrs.	—
Wm. J. Stewart.	Not published.	American, Jewish extraction.	16 yrs.	Male.	—	Brother has convulsions. Tuberculosis in ancestors.	Negative.	None.	No.	About 14 yrs.	Thyroid treatment increased mental alertness; did not accelerate growth.
S. Solis Cohen.	Not published.	American.	16 yrs.	Female.	—	None.	—	—	No.	About 10 yrs.	Improvement from anterior pituitary effect. Later fell back; but improved when thyroid extract was added.
J. C. Doan.	Not published.	American.	19 yrs.	Female.	—	None.	None.	—	No.	Not obtainable.	Improved after thyroid treatment, but at present growing worse.
M. B. Heyman.	Not published.	American.	28 yrs.	Female.	—	Both sides insanity; no thyroid disease.	None.	Episodes of excitement.	—	28 yrs.	Took thyroid at 22 years, little benefit derived. Stopped 1 year, then resumed, but developed hallucinations.

G. A. Smith.	Not published.	—	45 yrs.	Female.	Not enlarged.	Negative, except insanity.	None.	—	Yes.	Unknown.	No note that any treatment given.
Carl J. Hedin.	Not published.	—	—	—	Not palpable.	No thyroid disease. Mother highly neurotic. Tuberculosis in grandparents.	Mother took large amounts of "tansy tea" to abort child.	High-grade imbecile.	—	15 yrs.	Thyroid improved.
Carl J. Hedin.	Not published.	—	—	—	Not enlarged.	Both parents nervous.	None.	None.	—	Unknown.	No improvement.
G. A. Smith.	Not published.	—	—	—	Not enlarged.	—	None.	Insanity.	—	Unknown.	No note that treatment was ever given.
Geo. S. Bliss.	Not published.	American.	11 yrs.	Male.	—	—	—	—	—	—	—
Geo. S. Bliss.	Not published.	American.	13 yrs.	Male.	—	Mother very nervous.	—	—	—	—	—
Geo. S. Bliss.	Not published.	American.	28 yrs.	Male.	—	—	—	—	—	—	Improved on thyroid extract.
Geo. S. Bliss.	Not published.	American.	24 yrs.	Female.	—	Mother tuberculous.	—	—	—	—	Improved on thyroid extract.
Geo. S. Bliss.	Not published.	American.	22 yrs.	Female.	—	Mother very nervous.	—	—	—	—	Improved on thyroid extract.
Geo. S. Bliss.	Not published.	American.	28 yrs.	Female.	—	—	—	—	—	—	Improved on thyroid extract.
Martin W. Barr.	Not published.	American.	30 yrs.	Male.	Not enlarged.	—	—	—	No.	—	No marked benefit.
Martin W. Barr.	Not published.	American.	39 yrs.	Female.	Not enlarged.	Father died of tuberculosis.	—	—	No.	—	Not marked.
Martin W. Barr.	Not published.	American.	47 yrs.	Female.	Not enlarged.	—	—	—	No.	—	Not much benefit.
Martin W. Barr.	Not published.	American.	21 yrs.	Male.	Not enlarged.	—	Premature birth —weighed 3 lbs.	—	—	—	No marked effect.
Martin W. Barr.	Not published.	American. Parents Austrian.	18 yrs.	Female.	Not enlarged.	—	—	—	—	—	Under thyroid, learned to read, write and care for herself.
A. P. Busey.	Not published.	American.	13 yrs.	Female.	Absent.	Father alcoholic. Mother, maternal grandmother, one sister and two brothers have goiter.	—	—	No.	11 yrs.	Wonderfully benefited by thyroid extract.
Geo. A. Zellar.	Not published.	German.	55 yrs.	Female.	Not enlarged.	Negative.	Negative.	Delusions of persecution for 10 years.	No.	—	No special treatment given.

TABLE II—*Continued*

AUTHOR	REFERENCE	NATIVITY	AGE	SEX	CONDITION OF THYROID	HEREDITY	OTHER ETIOLOGICAL FACTORS	COMPLICATIONS	UNRECOGNIZED	DURATION	EFFECT OF TREATMENT
HUGH B. MEREDITH.	Not published.	American. German parentage.	28 yrs.	Male.	Atrophied and tuberculous at autopsy.	Negative.	Negative.	Marked idiocy	No.	Apparently congenital.	Improved under thyroid extract. Died at 30 years of pneumonia.
J. PERRY WADE.	Not published.	American.	22 yrs.	Male.	Not enlarged.	Negative.	Negative.	None.	No.	22 yrs.	Improved under thyroid.
J. N. SMITH.	Not published.	American.	16 yrs.	Male.	Not enlarged.	—	—	—	—	—	None.
J. N. SMITH.	Not published.	American.	14 yrs.	Female.	Not enlarged.	—	—	—	—	—	None.
J. N. SMITH.	Not published.	American.	14 yrs.	Female.	Not enlarged.	—	—	—	—	—	None.
G. W. BROWN.	Not published.	American.	64 yrs.	Female.	Not enlarged.	Negative.	Negative.	Syphilitic gumma.	—	62 yrs.	No treatment.
G. W. BROWN.	Not published.	American.	37 yrs.	Female.	Not enlarged.	Negative.	—	—	—	—	No treatment.
G. W. BROWN.	Not published.	American.	23 yrs.	Female.	Not palpable.	Negative.	—	—	—	—	No treatment.
G. W. BROWN.	Not published.	American.	18 yrs.	Male.	Not enlarged.	Father alcoholic	—	—	—	—	Thyroid extract had no effect.
G. W. BROWN.	Not published.	American.	17 yrs.?	Male.	Not enlarged.	Father tuberculous.	—	Manic-depressive attacks.	—	—	Pituitrin and thyroid without effect.
J. M. MURDOCK.	Not published.	American, Austrian parentage.	8 yrs.	Female.	Enlarged.	Unknown.	—	Idiot.	—	8 yrs.	Improvement.
J. M. MURDOCK.	Not published.	American, Austro-Hungarian parentage.	16 yrs.	Female.	Not enlarged.	Sister a cretin.	—	Imbecile.	—	16 yrs.?	Decided improvement.
J. M. MURDOCK.	Not published.	American, Austro-Hungarian parentage.	18 yrs.	Female.	Enlarged.	Sister a cretin.	—	Imbecile.	—	18 yrs.	Slight improvement.
J. M. MURDOCK.	Not published.	American.	30 yrs.	Female.	Not enlarged.	Unknown.	—	Imbecile.	—	30 yrs.	No perceptible improvement.
J. M. MURDOCK.	Not published.	American.	39 yrs.	Female.	Not enlarged.	Unknown.	—	Imbecile.	—	39 yrs.	Slight improvement.
J. M. MURDOCK.	Not published.	American.	14 yrs.	Male.	Not enlarged.	Unknown.	—	Idiot.	—	14 yrs.	Improvement.
J. M. MURDOCK.	Not published.	Unknown (Colored).	8 yrs.	Female.	Not enlarged.	Unknown.	—	Idiot.	—	8 yrs.	Much improvement.
J. M. MURDOCK.	Not published.	American.	38 yrs.	Male.	Enlarged.	Brother a cretin.	—	Imbecile.	—	38 yrs.	Slight improvement.
J. M. MURDOCK.	Not published.	American.	36 yrs.	Male.	Enlarged.	Brother a cretin.	—	Idiot.	—	36 yrs.	No improvement.

Nativity. The cretins, as shown by the table, were American-born, except that 1 was Italian, 1 Austrian, and 1 German-born, and 2 were of Austro-Hungarian parentage. The colored race furnished no examples of cretinism.

Age. Since sporadic cretinism develops in childhood or may be congenital, it was to be expected that the average age would be much below that of myxedema. This figure, however, is higher than has been anticipated, namely, 19.5 years, while the extremes noted in this table are sixty-four years and 3½ months, respectively. The average age for the females is twenty, and for the males eighteen years.

Sex. There were 28 males and 38 females, while in 7 the sex was unmentioned. The ratio of females to males is 1.4 to 1, whereas in myxedema it was that of 5 to 1. To account for the difference in the relative proportion of the cases between the sexes would at first sight appear to be difficult. Loss of function of the thyroid gland in myxedema, however, develops during or about middle life, and is in many cases intimately bound up with the condition of the female reproductive organs—a fact that has received special emphasis above. It cannot be claimed that disturbances of the generative functions alone are responsible for the differences in sexual incidence of myxedema and cretinism in the present state of our knowledge of the endocrine organs, but it is a potent modifying factor.

Condition of Thyroid. In 36 cases the condition of the thyroid gland was noted and in 4 instances was found enlarged. In 22 cases it is described as "not enlarged"; in 5 cases the gland was either not palpable or absent, while in 4 of the remainder described it was "small," or "atrophied."

Heredity. The column devoted to heredity shows that out of 41 cases in which the family history is given, in 5, or 11.5 per cent, goiter was noted among the parents or other near relatives. It is noteworthy that in one instance the mother and two of the sisters are goitrous; in another, one brother is a cretin, and an aunt has a goiter, in another one sister and in still another one brother are cretins; finally one example showed a maternal grandmother, one sister, and two brothers all afflicted with goiter.

The importance of alcoholism and tuberculosis as predisposing factors is about paralleled by their causative influence in myxedema. Syphilis in these collective observations is without noticeable effect. On the other hand, "nervousness" in the antecedents and collateral relatives was found in 4, and insanity in 2 cases. A more or less close relationship of cretinism to insanity, epilepsy, and "high-grade imbecility" is also shown by a glance at the table.

Duration. Attention should be called to the duration in relation to the age of the patients. The notations show clearly that the complaint is not

uncommonly a congenital one, e.g., in 25 cases of the present series. In view of this fact, it is not unreasonable to suppose that in true cretinism there is a degree of primary lack of embryonal development of the central nervous system which does not obtain in myxedema, and this anatomical and physiological defect may explain, in part at least, the differences in the results of treatment of the two conditions. Granting that this view may not be wholly warranted and overweighed by the evidence in favor of a common etiology for both cretinism and myxedema, yet it appears to be worthy of consideration. In a few instances only did cretinism appear to develop as a sequel of some acute infectious process.

Unrecognized. Of 31 cases in which there is a record made, the condition was unrecognized in 10, or 32 per cent—a smaller percentage than in the case of myxedema, most probably for the reason that cases of cretinism are more apt to fall under the care and observation of a specialist.

Diagnosis. The cases recorded in the accompanying table were observed by specialists whose diagnosis of the condition cannot in fairness be questioned. The responses in the majority of cases contained descriptive details, which set the question of diagnosis at rest. As stated above, there are types of idiocy other than that associated with cretinism, but the great majority of the photographs sent me showed typical cretins. The cases found in the literature of America and Canada and recorded in the table were also, with few if any exceptions, presumably examples of true cretinism.

Treatment. The column devoted to the effects of treatment shows that marked improvement occurred in 22 instances (about one-third the total number). Of the remaining cases, 9 showed slight beneficial effects and 8 no improvement. In only 1 case was a cure reported, whereas in connection with the subject of the treatment of myxedema, this term or its equivalent was employed in not less than 30 cases (more than half the total number). While the use of the thyroid extract is accompanied by marked beneficial effects in many cases of cretinism, the fact remains that on the whole its physical are far more satisfactory than its mental effects. Without further detailed analysis it is believed that anyone interested will find data for study in the table submitted on cretinism.

The points which need to be especially noted in connection with the subject of cretinism are: (*a*) That further growth of our knowledge of the etiology is desirable, despite the unbreakable etiological relationship with myxedema. (*b*) Cretinism in the male is relatively more common than myxedema, due largely to the dominating etiological connection of myxedema with the female reproductive

organs. (*c*) A decreased basal metabolic rate from any cause exercises a slight though definite predisposing influence. (*d*) The oft-repeated observation that cretinism may be an inheritance from goitrous antecedents receives confirmation from these statistical studies. (*e*) Thyroid preparations are less effective in cretinism, particularly with reference to the psychic manifestations, than in myxedema, although relatively more potent for good as regards the mental condition, if given in the earlier stages of the disease.

The writer is under obligations to H. Leon Jameson, M.D., and to Lieutenant Oscar Payne, M.D., for valuable aid in searching the American and Canadian medical literature for recorded cases of myxedema and cretinism.

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THE PIGMENT RING

By Edward B. Angell, Rochester, N. Y.,

Neurologist to the Rochester General Hospital

At the meeting of the Section of Nervous and Mental Diseases of the American Medical Association at Atlantic City, N. J., June, 1912, the author read a paper on the "Study of the Urine in Nervousness," which later was published in the *Journal of the American Medical Association*.[1]

Since that time the clinical value of this simple reaction has been emphasized in many hundreds of cases. No color scheme has heretofore been presented illustrative of this pigment ring. In the present communication, however, is reproduced a series of water-color designs accurately drawn from typical specimens, showing the variations in color of this reaction.

The pigment ring, as it may be termed, is found at the point of contact in a test tube, between the urine and the underlying nitric acid, replacing the white ring due to the presence of albumin—the so-called Heller's test. It is probably due to the oxidizing influence of the nitric acid upon the end products of protein katabolism. The exact chemistry of this reaction, however, has not yet been determined. As is well known, the investigation of these end products of proteid metabolism is associated with much difficulty, and their chemistry is yet far from clear. The reaction, however, is very definite, and of much clinical significance in relation to nervousness or the neurasthenic syndrome.

The pigment ring varies from a slightly brownish yellow, which may be called the normal pigment ring, Fig. 1, to a deep brown, Fig. 2, or a bright carmine, Fig. 3. Doubtless the urine of the normal individual also gives a moderate color reaction to the same reagent, depending somewhat upon the habits of the individual so far as food, muscular activity, and occupation are concerned.

[1] November 16, 1912, LIX, 1775-1777.

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Indeed, the suggestion has been offered that a pronounced pigment ring has been found in the urine of healthy individuals not suffering from any disorder of the nervous system. This undoubtedly is true. The reaction does indicate, however, that there is a disturbance in the normal metabolism of the individual, either an undue ingestion of protein or an interference with normal elimination. As the result of this chemical disturbance of protein metabolism, the nervous system becomes irritable and the mental tone depressed more or less noticeably. Then some mishap occurs, an accident, financial loss, a painful affliction, or perhaps a disorder like influenza. The sufferer becomes nervous, depressed, and the so-called neurasthenic state develops. The condition is ascribed to the mental shock or worry, not to its true cause—the disturbed metabolism of the nervous system. It is in reality a disorder of the brain rather than of the mind, and should be treated by physical methods rather than tonics, rest cure, or psychotherapy. Its dominant manifestation is subjective phenomena, the patient being altogether too conscious of his feelings owing to the depressed tone of his mind.

A careful neurological examination of the patient usually gives a negative result. No structural change can be discovered, the whole category of symptoms being subjective in character. The "bill of complaints" reveals a long train of aches, headache, backache, leg ache, vertigo, irritability, sleeplessness, extreme fatigue, lack of will-power, an emotional condition hardly controlled, even apprehension of loss of mind or death. The list is by no means exhausted, and varies somewhat in accordance with the personality of the individual, but this train of symptoms forms a picture of nervousness often presented to the practitioner.

These are the cases that can readily be cured, not by confinement to the bed and the use of electricity and massage, but by wholesome out-of-door activity, aided by a generous diet limited in proteids and fed on the salicylate of sodium in moderate doses.

The four examples here reproduced well illustrate the color reaction at the point of contact between the urine and the nitric acid.

No. 1 is that of a normal pigment ring, subsequent to efficient treatment.

No. 2 shows the dark-brown ring often associated with indican, taken from a patient who was referred with a diagnosis of "brain

tumor." The neurological examination disclosed no organic trouble, and the condition, as well as the reaction of the urine, was promptly cleared up by the use of the salicylates, an alkali, and adherence to a proper diet.

No. 3 is the bright carmine ring often noticed in pale urines. This was a specimen from a patient with nervous depression, associated with vertigo, headache, marked irritability, weariness, and fear of impending death. Thorough examination disclosed no organic trouble. The symptoms were largely subjective and disappeared, as did the pigment ring in the urine, under the prescribed regimen.

No. 4 shows the pigment ring found in the urine of patients taking iodide of potassium. Potassium iodide also causes this reaction, but usually the ring is better defined than the ordinary pigment ring, and the presence of the iodides can readily be determined.

No. 5 shows the highly colored pigment ring associated with too rich a protein diet, occurring in a urine that was highly acid and of a high specific gravity.

Indican, iodide of potash, and biliary pigments may be present in the urine, but their presence is not essential, as is shown by means of differential tests, nor is this reaction affected by the presence in the urine of urea or uric acid.

Undue acidity of the urine is usually found associated with this condition. Whether it is significant of an increased acidity of the blood cannot be asserted. There seems, however, some relation between acidosis and many of the subjective symptoms of nervous depression.

It is well to bear this in mind in the management of this class of cases, and by some of the alkalies reduce any hyperacidity of the urine to a minimum.

Persistent treatment by the use of some one of the salicylates for a period of three to six months is often required to clear up the nervous symptoms and restore the normal pigment line. It is, indeed, true that a few of these cases are true neurasthenics, while some show the persistent obsessions of a distorted mind—nervous folk who will respond only to more systematic methods.

SYMPTOMS AND SIGNS OF HELP IN CLINICAL RECOGNITION OF GENERAL AND REGIONAL ATHEROSCLEROTIC PROCESSES

By Lewellys F. Barker, M.D., Baltimore, Md.

THE clinician in whose honor this volume is published gave clear evidence of an especial interest in the clinical manifestations and the underlying anatomical and pathological-physiological foundations of the several conditions that together are described as arteriosclerosis, or atherosclerosis. This interest has always been exhibited in both his practice and his teaching, and is also shown in several of his publications, notably in the chapters on arteriosclerosis in his "Principles and Practice of Medicine," and in "Modern Medicine," in his paper entitled, "Transient Attacks of Aphasia and Paralysis in States of High Blood Pressure and Arteriosclerosis," and in his volume on "Angina Pectoris." And it is on account of his belief in the practical importance of the subject and the attention that he gave to it that I decided, when invited to contribute to this volume, to try to bring together, in a brief but systematic way, the main criteria that clinically help us in the detection in our patients of existing atherosclerotic processes, general or regional.

Without discussion here as to the nature of the atherosclerotic process, or as to the sequence of events in its development, I shall, for the purpose of the present paper, arbitrarily include under the designation "atherosclerosis" not only (1) the clinical conditions in which organic changes in the arterial walls can be recognized by palpation during the life of the patient, but also (2) certain clinical conditions (e.g., angina pectoris, pseudobulbar paralysis, etc.) that have been shown by post-mortem control to depend, in many instances at least, upon atherosclerotic changes, as well as (3) certain other clinical conditions (e.g., arterial hypertension and vascular crises) that may, in the earlier stages, perhaps, be unassociated (even at autopsies secured through death from intercurrent diseases)

with as yet demonstrable anatomical changes in the arterial system. It will be understood, then, that the marks here collected include those useful in the detection not only of cases of the so-called "decrescent atherosclerosis" without hypertension, but also of cases of arterial hypertension with, or without, demonstrable arterial thickening, including the so-called "essential hypertension" or "hyperpiesis" of Sir Clifford Allbutt. I do not include under atherosclerosis the changes due to luetic arteritis or to other forms of infectious arteritis. The attempt will be made here to summarize the chief clinical phenomena that may be met with in one or another stage of a general, or of a local, atherosclerotic or pre-sclerotic process, laying special emphasis upon the distinctive marks that point to a regional, an organal, or a focal nutritional involvement. My own clinical experience has taught me the importance, on recognizing a mark of possible atherosclerosis in one domain, of looking most carefully for the marks that point to other single domains, or to a generalized process. It is hoped that a succinct tabulation of the marks that may be present in various atherosclerotic states may be found convenient to clinical workers.

ATHEROSCLEROSIS OF THE AORTA

We know from the studies of the pathological anatomists that, in the aorta, it is the aorta abdominalis that is most often and most severely affected by atherosclerotic processes; next in frequency and severity of involvement comes the descending aorta thoracalis; and lastly, the aorta ascendens and the arcus aortæ.

The atherosclerotic process consists in the development of two principal changes: (1) a primary *fatty degeneration* beginning in the tunica intima; and (2) a secondary, compensatory (?), *sclerotic proliferation*, in which a layer of new connective tissue is formed just beneath the surface endothelium, this new tissue separating the endothelium and the lumen from the underlying area of intima cells that have undergone fatty degeneration, and that are also, sometimes, the site of associated deposits of cholesterin and calcium. In the early stages of the process, when there is only a slight fatty change in the tunica intima of the aorta, clinical recognition is not possible; in the more advanced stages with multiple atheromatous foci and loss of elasticity of the aortic wall, the aorta becomes elongated and

undergoes dilatation (diffuse or circumscribed), and clinical recognition becomes possible. Occasionally, aneurysmal dilatation occurs and, sometimes, multiple aneurysms of the aorta develop, though far less frequently than in luetic aortitis. In advanced atherosclerosis of the aorta, an atheromatous ulcer may occasionally rupture and give rise to a dissecting aneurysm (or intramural hematoma).

Aorta Ascendens and Arcus Aortæ. Atherosclerosis of these portions of the aorta can often be recognized clinically by the presence of some of the following marks:

(1) *Signs of Diffuse Dilatation and Elongation.* (*a*) Visible pulsation in the episternal notch; (*b*) visible lift of the manubrium; (*c*) visible pulsation in the first and second intercostal spaces near the sternum; (*d*) retromanubrial and paramanubrial dullness; (*e*) high position of the subclavian arteries; (*f*) bell-like, ringing aortic second sound; (*g*) pressure symptoms (dilatation of veins of upper thorax, dyspnea, tracheal tug, anisocoria, etc.), but these are less frequently present than in aneurysm; (*h*) visibly increased width of the shadow of the aorta, persisting between pulsations, on roentgenoscopic examination; (*i*) transverse position of the heart (on roentgenoscopy and in the teleroentgenogram). Of these signs, by far the most important for quick clinical recognition are (1) retromanubrial dullness and (2) the *x*-ray evidence of dilatation and elongation. The blood pressure may, or may not, be increased in diffuse dilatation of the aorta due to atherosclerosis.

(2) *Signs of Aortic Insufficiency or of Aortic Stenosis.* In the absence of lues and of a "rheumatic" history, the existence of aortic insufficiency, or of aortic stenosis, in a person of middle or later life, are marks strongly suggestive of aortic atherosclerosis extending to the valvulæ semilunares.

(3) *Symptoms of Angina Pectoris.* The occurrence of retrosternal pain on exertion is a mark that points to the coronary circulation (*vide infra*), but it should be kept in mind that the coronary circulation may be impeded by atherosclerotic changes of the aorta at the orifices of the coronary arteries in the sinuses of Valsalva. Sir Clifford Allbutt leans to the view that changes in the aorta are the only constant findings in angina pectoris, despite the generally accepted opinion that angina pectoris is most often due to sclerosis of the coronary arteries.

(4) *Symptoms and Signs of Aortic Aneurysm.* Aortic aneurysm may be due to atherosclerosis of the aorta, though more frequently to luetic aortitis. Under the fortieth year, aneurysm of the aorta is nearly always infectious, rarely atherosclerotic, in origin; after that age it may be either infectious (luetic) or atherosclerotic in origin. The marks of *aneurysm of the aorta ascendens* include: (*a*) visible pulsation or swelling; (*b*) palpable expansile pulsation in the second right intercostal space with diastolic shock; (*c*) dullness to the right of the manubrium with increased resistance; (*d*) dislocation of the heart to the left; (*e*) pulsating, expansile, sharply circumscribed shadow more to the right than to the left of the sternum in the anterior thorax on roentgenoscopic examination of the cardiovascular stripe. The marks of *aneurysm of the arcus aortæ* include: (*a*) tracheal tug; (*b*) symptoms of pressure upon trachea, left bronchus, N. recurrens, N. sympathicus, esophagus or spine (cough with unclosed, or imperfectly closed, glottis; paroxysmal dyspnea; hoarseness; laryngeal stridor; laryngoscopically visible unilateral paralysis of vocal cord; anisocoria; dysphagia; pain); (*c*) abnormally pulsating, sharply circumscribed shadow to the left of the sternum, above the heart, on roentgenoscopic examination.

Aorta Descendens (Thoracalis). The marks of *diffuse dilatation of the aorta descendens* (*thoracalis*) include (*a*) paroxysmal intercostal neuralgia (unilateral or bilateral), probably indicating involvement of the orifices of the *Aa. intercostales* or of the walls of these arteries somewhere in their course; and (*b*) visible dilatation of the descending aorta on roentgenoscopic examination of the thorax with oblique transillumination. The marks of *aneurysm of the aorta descendens* (*thoracalis*) include: (*a*) dysphagia; (*b*) pain in the back and along the sides; (*c*) expansile pulsating area in the left back; (*d*) symptoms and signs of compression of the left lung; (*e*) pulsating, expansile, circumscribed shadow to the left of the sternum in the posterior thorax on roentgenoscopic examination.

Aorta Abdominalis. Atherosclerosis of this part of the aorta, though exceedingly common as a post-mortem finding, is only occasionally clinically recognizable. In emaciated patients, however, with thin and relaxed abdominal walls, a *tortuous rigid abdominal aorta* can be palpated; occasionally its outline is actually visible.

When an *aneurysm due to atherosclerosis of the abdominal aorta*

exists the clinical marks of it may be very characteristic, even in patients that are not thin. They include: (*a*) persistent and intense abdominal pain; (*b*) visible abdominal pulsation; (*c*) a "definite tumor, which can be grasped and which has an expansile pulsation"; (*d*) retardation of the pulse in the A. femoralis; (*e*) persistence of the pulsation in the knee-elbow position; (*f*) arterio-systolic bruit.

The throbbing aorta of neurasthenic states, of anemia, and of exophthalmic goiter is easily distinguishable from aneurysm. In the abdomen, as elsewhere, aneurysm before forty is usually luetic or mycotic in origin; and aneurysm of atherosclerotic origin is rare until after middle life.

ATHEROSCLEROSIS OF THE CORONARY ARTERIES

Several remarkable clinical phenomena may make their appearance in association with atherosclerosis of the coronary arteries. The most striking of these are: (1) attacks of "angina pectoris"; (2) attacks of "cardiac asthma"; (3) certain phenomena dependent upon "myomalacia cordis" and its sequels (aneurysms of the heart; fibrosis myocardii).

The marks of a severe *attack of angina pectoris* or *stenocardiac attack* include: (*a*) sudden agonizing pain (on exertion or on excitement) in the region of the heart or behind the breastbone (dolor pectoris) often radiating to the neck and (left) arm; (*b*) a sense of constriction in the chest as though the heart or the chest wall were grasped and being compressed; (*c*) a feeling of intense anxiety and of impending death ("angor animi"); (*d*) pallor of the face, or an ashy-gray tint, with sweating; (*e*) when an area of cardiac muscle undergoes softening (myomalacia), there may be pericarditic symptoms in a few days after the paroxysm if the softening reaches the pericardium. In mild attacks there may be only retrosternal oppression. In atypical attacks the pain may begin outside the chest (extra-pectoral pain), in the arm, in the jaw, in a tooth, in one testis, in the occipital region, in one kidney, or in the epigastrium (angina abdominis).

In persons under forty attacks of angina pectoris are often due to luetic aortitis with narrowing of the orifices of the coronary orifices, rarely to true atherosclerosis. After forty, the attacks may be due to narrowing of the orifices of the coronary arteries due either

to luetic aortitis or to aortic atherosclerosis, or they may depend upon atherosclerotic changes in the coronary arteries themselves anywhere in their course. It is probable that attacks may occur from spasm of the coronary arteries before any outspoken atherosclerotic changes are demonstrable in these vessels.

The marks of an attack of *asthma cardiale* include: (*a*) a sudden severe paroxysm of dyspnea (orthopnea) with noisy respiration, coming on most often in the night after going to sleep, though sometimes following immediately upon physical exertion, strong emotion, or a hearty meal; (*b*) a feeling of constriction of the neck and of severe oppression in the chest; (*c*) the signs of more or less pulmonary edema (fine and coarse moist râles over certain areas of the lungs, especially both bases; expectoration absent, or containing very tough brownish mucus; less often greater or smaller amounts of frothy, blood-tinged sputum); (*d*) small, soft pulse, often with marked tachycardia and sometimes with arrhythmia; (*e*) not infrequently, widening of the area of cardiac dullness in the attack, with pain and tenderness in the region of the liver.

The marks of *myomalacia cordis and its sequels* are less distinctive than are those of angina pectoris and of asthma cardiale, for this degenerative myocardiopathy of vascular origin (myomalacia followed by scarring) may be closely simulated in symptoms and signs by the toxic-degenerative myocardiopathies (and myocarditides). The marks include : (*a*) symptoms and signs of chronic circulatory insufficiency in the general and in the pulmonary system (especially when associated with any of the marks of atherosclerosis of the aorta or aortic valves, or with other marks of coronary sclerosis, such as angina pectoris and asthma cardiale); (*b*) persistent bradycardias without other signs of vagotonia; (*c*) cardiac arrhythmia; (*d*) abnormalities in the electrocardiogram; (*e*) rarely, the clinical and roentgenological signs of aneurysm of the heart, situated nearly always in the left ventricle near the apex; (*f*) still more rarely, rupture of the heart.

The time is scarcely yet ripe for a full discussion of the marks for distinguishing (1) lesions of the right coronary artery from lesions of the left coronary artery, (2) lesions of the single rami of each coronary artery, and (3) secondary lesions of different areas of the cardiac muscle. We are fast approaching that time, however, and we already possess certain clues

that will be helpful in the construction of a practical schema for topical diagnosis in coronary and myocardial domains. Thus, in general, it has been found that the atherosclerotic process affects the *A. coronaria sinistra* more often and more severely than the *A. coronaria dextra.* In the few cases in which the right artery has been more involved than the left, it is asserted that the right ventricle was markedly enlarged and the left ventricle was not increased in size. Sudden death in an attack of angina pectoris or of cardiac asthma may point to thrombosis of one coronary artery or of an important ramus, secondary to atherosclerotic change, but not necessarily. Thus sudden death has been known to follow closure (1) of either coronary artery at its aortic orifice, (2) of the ramus circumflexus, or (3) of the ramus descendens anterior of the left artery, as well as (4) of the ramus descendens posterior of the right artery. Death does not always follow closure of such a vessel by disease or on experimental ligation. The commonest site of myocardial scarring, of heart aneurysm, and of heart rupture is the anterior surface of the left ventricle near the apex, an area supplied by the *ramus descendens anterior of the left coronary artery.* Electrocardiography and the newer pathological physiology and anatomy of the conduction-system in the heart are supplying rapidly the data that we may use for a topical diagnosis of myocardial disease. Polygraphic tracings opened the way to this new and important field of research.

ATHEROSCLEROSIS OF THE ARTERIES OF THE HEAD

The arteries of the head include: (1) the A. carotis externa of each side and its branches; (2) the A. carotis interna of each side and its branches; and (3) the A. vertebralis of each side and the unpaired A. basilaris (resulting from their union) and their branches.

Arteria Carotis Externa. The marks of atherosclerosis in the domain of this artery and its branches include: (*a*) palpable thickening of the A. maxillaris externa where it bends over the basis mandibulæ at the anterior margin of the masseter muscle; and (*b*) visible tortuosity or palpable thickening of the ramus frontalis of the A. temporalis superficialis in the temple.

Arteria Carotis Interna. Atherosclerosis of the main trunk of this artery may sometimes cause symptoms and signs, owing to (*a*) pressure of the dilated and rigid vessel wall on the N. opticus or on the eye-muscle nerves; (*b*) aneurysm of the atherosclerosed vessel compressing the same nerves, the tractus olfactorius or the ophthalmic division of the trigeminus (amblyopia, oculomotor paralysis,

sensory disturbances about the eye, nose, and forehead, anosmia, etc.); or (*c*) thrombosis of the atherosclerotic vessel.

The main branches of the internal carotid artery are (1) the ophthalmic artery and (2) the anterior and middle cerebral arteries. The marks of atherosclerosis sometimes recognizable in the domain of the *A. ophthalmica* and its branches include: (*a*) arcus senilis in the cornea; (*b*) thrombosis of the arteria centralis retinæ; (*c*) ophthalmoscopically visible atherosclerosis of the small retinal arterioles (tortuosities, indentations, whitish margins along the arterioles, thickenings, localized narrowings of the blood-column, obliterations, thromboses, minute hemorrhages, yellowish spots due to degeneration of the lamina vitrea of the chorioid); (*d*) glaucoma; (*e*) intractable senile catarrhal conjunctivitis; aneurysm with exophthalmus pulsans.

The marks of atherosclerosis in the domain of the *arteriæ cerebri* derived from the A. carotis interna include: (*a*) the symptoms of general atherosclerosis of these cerebral vessels (headache, matutinal insomnia, dizziness, memory defect, irritability, lack of emotional control, epilepsia tarda, in later stages, dementia); (*b*) the pseudobulbar-paralysis syndrome (supranuclear dysarthria, dysphagia, dysmasesia, explosive laughing and crying, drooling, walking with little steps, etc.); (*c*) focal signs and symptoms due to narrowing, to thrombosis with encephalomalacia, to aneurysm, or to hemorrhage in the domain of the single branches, say the *arteria cerebri anterior* (monoplegia cruralis; anosmia), or the *arteria cerebri media* (contralateral hemiplegia and hemianesthesia, motor aphasia, sensory aphasia, etc.). Lesions of the *posterior branch of the third division of the left A. cerebri media* cause pure, or subcortical, alexia with hemianopsia (or hemiachromatopsia) dextra. The *lenticulostriate and lenticulo-optic arteries*, lesions of which cause injury to the capsula interna, are branches of the A. cerebri media.

Arteria Vertebralis. The marks of atherosclerosis in the branches of this artery include: (*a*) signs of *atherosclerosis of the A. spinalis posterior* and of the *A. spinalis anterior* supplying the spinal cord (senile spastic paraparesis with sensory and sphincteric disturbances; senile paraparesis with enfeeblement of deep reflexes); (*b*) signs of *narrowing* or *thrombosis of the arteria cerebelli inferior posterior* (unilateral palatal and laryngeal paralysis, dysphagia, contralateral

hemianesthesia [thermanesthesia and analgesia] homolateral trigeminal anesthesia, sometimes cerebellar ataxia, etc.); (*c*) signs of *aneurysm of the trunk of the A. vertebralis* (rarer than aneurysm of A. basilaris mentioned below, but yielding similar symptoms and signs, especially unilateral bulbar paralysis with homolateral hemianesthesia and contralateral hemiplegia).

Arteria Basilaris. The marks of atherosclerosis in this artery and its branches include: (*a*) signs of *tortuosity, rigidity, and dilatation* and of *aneurysm of the A. basilaris* compressing the pons, medulla oblongata, and cerebral nerves (occipital pain; limited motility of the head; miosis; pupillary rigidity; attacks of anarthria, dysphagia, dyspnea, tachycardia and arrhythmia; paralyses of the V, VII, VIII, IX, X, XI and XII cerebral nerves; unilateral convulsions; hemiplegia alternans; and, sometimes, hemianesthesia and hemiataxia); aneurysm here, as elsewhere, is, however, more often due to luetic arteritis than to atherosclerosis; (*b*) signs of *thrombosis of the A. basilaris* and *A. vertebralis* with softening in the pons and medulla (acute bulbar paralysis with paraplegia of all four extremities); (*c*) signs of *atherosclerosis of the cerebellar arteries* (atherosclerotic form of cerebellar ataxia,—"drunken gait" with asthenia, atonia and astasia); (*d*) signs of *atherosclerosis of the A. auditiva interna* with injury to the cochlear and vestibular apparatus and paths (labyrinthine deafness and attacks of aural vertigo; abnormal findings with Bárány tests); (*e*) signs of *atherosclerosis of the A. cerebri posterior* with its branches, especially of the *arteria occipitalis of Duret* supplying the visual areas of the cortex (cortical hemianopsia; cortical blindness; mind blindness; when the left artery is involved, optic aphasia), and of the *arteria temporalis of Duret* supplying the gyrus hippocampi and the uncus (cortical anosmia; olfactory hallucinations; "uncinate gyrus fits"), though these areas are also partly supplied by a branch of the A. cerebri media. The *main trunk of the A. cerebri posterior* may become narrowed (attacks of vertigo, temporary hemianopsias, scintillating scotoma with headaches and temporary amblyopia) and, later, occluded (coma followed by hemiplegia, which may subsequently clear up; there is often a residual hemianopsia and, in case of the left artery, a residual sensory aphasia or paraphasia, and amnesic aphasia); and (*f*) signs of *atherosclerosis of the rami ad pontem* (symptoms and signs of pontile nuclear and

supranuclear lesions, of pyramidal tract lesions, of lesions of the lemnisci, and of lesions of the brachia conjunctiva, brachia pontis and corpora restiformia).

ATHEROSCLEROSIS OF THE ARTERIES OF THE EXTREMITIES

The marks of *atherosclerosis of the arteries of the extremities* include: (*a*) visible tortuosity and dilatation of certain of the arteries (*A. brachialis*; *A. radialis*; *A. ulnaris*; *A. femoralis*); (*b*) palpable rigidity, thickening, and sometimes, calcification of the walls of accessible arteries; thus, thickened radials or "goose-neck" radials should always be felt for; (*c*) shadows of tortuous, calcified arteries in roentgenograms (legs; arms); the calcified nodules in Mönckeberg's medial sclerosis of the femoral arteries should show in roentgenograms; (*d*) disappearance of the pulse normally palpable in some of the smaller peripheral arteries (e.g., *A. dorsalis pedis* on the dorsum of the foot and the *A. tibialis posterior* below and behind the medial malleolus); (*e*) signs of *aneurysm of the A. subclavia* (expansile pulsating mass in the supraclavicular fossa; enfeeblement and retardation of homolateral radial pulse; symptoms of pressure on the brachial plexus); of *aneurysm of the A. femoralis* (pulsating, expansile mass in the course of the artery; change in pulse in arteries distal to it); of *aneurysm of the A. poplitea* (pain behind the knee; pulsating mass in popliteal space; neuralgias and paresthesias in the leg; maintenance of the knee-joint in partial flexion); any of these aneurysms may be due to atherosclerosis, though aneurysms of traumatic and of luetic origin are commoner in the arteries of the extremities than are aneurysms of atherosclerotic origin; (*f*) signs of *narrowing of the arteries leading to motor, sensory, vasomotor, and trophic phenomena* (intermittent limping or claudication, or dysbasia angiosclerotica, with pains, paresthesias, acrocyanosis, or pallor on use of the extremities; muscular cramps; localized muscular atrophies; erythromelalgias; symmetrical gangrene or Raynaud's disease; atherosclerotic "neuritides," or neurodegenerations, with spontaneous pains, hyperesthesias and anesthesias; acroparesthesias; persistence of pallor after removal of an Esmarch bandage); (*g*) signs of *occlusion of arteries in the extremities* (senile gangrene; diabetic gangrene).

ATHEROSCLEROSIS OF THE VISCERAL RAMI OF THE ABDOMINAL AORTA

The principal arteries to be considered here are the A. celiaca, the A. mesenterica superior, the A. mesenterica inferior, the A. suprarenalis media, the A. renalis, the A. spermatica interna, the A. testicularis, the A. ovarica, and the branches of these several arteries. Though any or all of these arteries may be involved in the atherosclerotic processes, as autopsies have shown, the marks for the clinical recognition of atherosclerosis of these arteries remain for the most part yet to be discovered. In certain instances, however, there are clinical signs and symptoms that point to, or suggest, atherosclerosis, and these may now be mentioned.

The Celiac Artery and its Branches. The short trunk of the A. celiaca splits up at the upper margin of the pancreas into three vessels, the A. gastrica sinistra, the A. hepatica, and the A. lienalis. The marks of atherosclerosis in this domain include: (*a*) symptoms and signs of *aneurysm* (abnormal pulsation; palpable, expansile mass; bruit; epigastric pain; vomiting; hematemesis; melena), but often difficult or impossible to distinguish from aneurysm of the abdominal aorta. In aneurysm of the A. lienalis the mass may be deep in the left hypochrondrium. The symptoms of aneurysm of the hepatic artery are usually believed during life or before operation to be due to gall stones, cholecystitis, or duodenal ulcer; it may be associated with chronic jaundice and intestinal hemorrhage.

The Mesenteric Arteries and Their Intestinal Branches. The marks of atherosclerosis in this domain include: (*a*) the syndrome known as "*dyspragia angiosclerotica intermittens*," characterized by paroxysms of severe abdominal pain occurring in atherosclerosis; (*b*) symptoms and signs of *thrombosis of a mesenteric artery with infarction* of a section of the intestine (colicky pains; vomiting; bloody stools; distention); the condition is often mistaken for acute peritonitis, or for intestinal obstruction due to other causes, until operation or until autopsy; (*c*) symptoms and signs of *aneurysm of a mesenteric artery* (similar to those of aneurysm of the abdominal aorta (q.v.); though the mass may be more movable, there is no retardation of the pulse in the femoral arteries, and the *bruit* may be less well propagated along the course of the aorta).

The Arteries Supplying the Pancreas. These include the superior and inferior pancreatico-duodenal arteries and the pancreatic rami of the splenic artery. The marks of atherosclerosis of these vessels include: (*a*) signs and symptoms of so-called "*pancreatic apoplexy*," in which there is hemorrhage into the pancreas and necrosis (sudden severe pain in upper abdomen with collapse, tachycardia and fall of blood pressure, occurring in an obese person of middle or later life; rigidity of abdominal muscles at first; later, palpable diffuse resistance; diagnosis rarely certain before operation); (*b*) signs and symptoms of the *atrophic granular form of pancreatic cirrhosis* (insufficiency of the internal secretion, shown by diabetes mellitus; insufficiency of the external secretion, shown by bulky, fatty stools and by deficiency of pancreatic ferments in duodenal contents obtained by duodenal pump).

The Renal Arteries. The main trunks, the interlobar arteries, the afferent glomerular vessels and the arteriolæ rectæ may be simultaneously, or more or less separately, involved. The marks of atherosclerosis in this domain include: (*a*) those of the *coarsely scarred atherosclerotic kidney*, or *focal form of atherosclerotic nephropathy* (slight polyuria, transient albuminuria, and cylindruria, rather high specific gravity of the urine, a few red corpuscles in the urinary sediment, blood pressure not always increased, no marked renal insufficiency); a similar kidney can result from multiple-healed infarctions following embolism; (*b*) those of the *genuine contracted kidney* or *diffuse arteriolar* (*sclerotic*) *nephropathy* (polyuria; low specific gravity of the urine; a trace of albumin and a few hyaline casts in the urine; chronic arterial hypertension, and hypertrophied heart). This is a part of the general sclerosis of the small arterioles of the organs (*vide infra*); (*c*) those of *aneurysm of the renal artery* (pulsation, bruit), though aneurysm here is most often traumatic in origin rather than atherosclerotic; (*d*) those of *thrombosis of the atherosclerotic renal artery* with complete or partial necrosis of the kidney (this cause of renal infarction is very rare).

Atherosclerosis of the Pulmonary Arteries

This condition is not infrequently seen at autopsy, but is rarely recognizable during life. The clinical marks that may be present in

cases in which the pulmonary arteries are much constricted from atherosclerotic change include: (*a*) accentuation of pulmonary second sound; (*b*) enlargement of right ventricle on percussion and in the teleroentgenogram; and (*c*) in late stages, signs of insufficiency of the right ventricle (dyspnea; marked cyanosis).

SCLEROSIS OF THE ARTERIOLES AND OF THE CAPILLARY VESSELS

Clinically, this is by far the most important form of disease of the blood vessels, for it is the form that is associated with arterial hypertension, with hypertrophy of the heart, with cerebral apoplexy, with renal insufficiency and with various disturbances that result from the malnutrition of organs fed by narrowed arterioles, especially in splanchnic, renal, and cerebral domains. The clinical marks of this condition, which I am accustomed to designate *arteriolar sclerosis* (described by Gull and Sutton as "*arterio-capillary fibrosis*," and by Jores as "*sclerosis of the small organ arterioles*") include:

(*a*) in the *early stages* (often a preternatural feeling of well-being and excessive business or professional activity; a trace of albumin or a few casts in the urine, found accidentally on examination for life-insurance or at a regular, periodic diagnostic survey maintained as a preventive measure; systolic and diastolic blood pressures somewhat variable around the upper limits of "normal" or a little higher; slight nocturia; slight polyuria); (*b*) in the *stage of outspoken arterial hypertension* (systolic blood pressure 150 to 190, diastolic 70 to 100; forcible apex-beat; accentuated aortic second sound; urine negative except for occasionally a trace of albumin and a few hyaline casts; moderate polyuria, both day and night; phthalein test of renal function usually reveals normal elimination or even "hyperpermeability"; the states often referred to as "hyperpiesis of Sir Clifford Allbutt" or as "essential arterial hypertension" probably belong here); (*c*) in an *advanced stage, but before serious complications have occurred* (systolic blood pressure above 200, diastolic above 100; demonstrable enlargement of the left ventricle of the heart (the "Traube heart"); markedly accentuated aortic second sound; nocturia; polyuria; urine, pale, of low specific gravity, with fixation of the latter, "hyposthenuria"; headaches; feeling of pressure in the head; attacks of slight dizziness; epistaxis; slight dyspnea on exer-

tion); (*d*) in an *advanced stage with serious complications* (in addition to the signs and symptoms described under (*c*), there may be the marks of (1) *myocardial insufficiency* (dyspnea; sometimes Cheyne-Stokes respiration; cyanosis; dilatation of the heart; gallop rhythm; anasarca; enlargement and tenderness of the liver; diminution of urinary output with marked albuminuria; pulmonary edema; asthma cardiale, etc.); of (2) *uremia*, due to the superimposition of a stasis-nephropathy or of a toxic-degenerative or of an inflammatory nephropathy upon the kidneys already sclerosed and contracted from the arteriolar (sclerotic) nephropathy (headache, dimness of vision, heavy foul breath, anorexia, nausea, vomiting, diarrhea, pruritus, mental dullness, drowsiness, delirium, twitchings convulsive seizures, temporary paralyses, coma, "albuminuric retinitis," retinal hemorrhages, lessened urinary output with albumin and casts, high blood-nitrogen, acidosis revealed by alveolar-air test, marked diminution of phthalein output, marked increase of ureo-secretory constant of Ambard, etc.); of (3) *cerebral apoplexy* ("stroke"; focal symptoms; residual symptoms); or of (4) *terminal infection* (pneumonia; pleuritis; colitis; general sepsis).

From the above analysis it is obvious that clinicians are now familiar with a great number of signs and symptoms, any one of which may serve as a mark to direct the attention toward a regional or a general atherosclerotic process.

STUDIES ON MALARIA CONTROL

THE FREQUENCY OF MALARIA RELAPSE IN AN AREA OF GREAT PREVALENCE IN THE MISSISSIPPI DELTA[1]

C. C. Bass, M.D.

(From the Department of Experimental Medicine, Tulane Medical College, New Orleans)

A DEMONSTRATION in control of malaria by treating malaria carriers, in Sunflower County, Mississippi, during 1918, has afforded an opportunity of making observations and collecting data which shed light upon the frequency of malaria relapse among the particular group and class of people under observation. It is not at all certain, nor in fact probable, that the frequency of relapse indicated by the data in this group of people is the same as it is in all other groups and classes where malaria prevails. It is probable, however, that this is fairly representative of the frequency in a large part of the malaria area of the United States.

Whether an individual who has an attack of malaria relapses following an attack or not depends very largely upon the thoroughness of the quinine treatment received. It is assumed that all who are informed upon the subject will agree with the statement that any person may be disinfected of malaria parasites by proper quinine treatment for sufficient length of time. Such an individual, of course, could not relapse. On the other hand, any person who retains malaria parasites, following an attack and insufficient treatment, may relapse. However, not all such persons do relapse. Some finally lost their infection without ever having any recognized symptoms and without taking any treatment for it whatever. It is quite likely that this elimination of infection, independent of specific

[1] This is one of a series of papers to be published, based largely or entirely upon malarial control work, conducted jointly by the International Health Board and the Mississippi State Board of Health.

treatment, varies greatly with different groups of people as the result of climate, race, habits of life, and perhaps many other factors. It also varies in different individuals. It should be appreciated, therefore, that the indications pointed out by these observations are only applicable to people under the same influences, so far as malaria relapse is concerned, as the people upon whom they were made.

The observations referred to here were made upon people living in an area of 100 square miles in the central portion of Sunflower County, Mississippi. Sunflower County is a typical Mississippi delta county. The rich alluvial soil is poorly drained, and was built by the overflows of the Mississippi River through past ages. The uncleared areas are covered with dense forests of hardwood, chiefly oak, ash, and gum. In many places there is a dense undergrowth of bushes, vines, etc.

The population of the area studied averages 90 per square mile, consisting of 17.8 per cent whites and 82.2 per cent negroes. The chief industry is growing cotton. This is generally done by so-called "one-horse" methods with "the negro and the mule."

The wide prevalence of malaria in the area is indicated by the fact that of 7089 persons from whom a careful history was obtained, 41.33 per cent gave a history of one or more attacks of malaria during the previous twelve months, and of those who gave negative histories, 18.78 per cent were found to have malaria parasites upon blood examination.

A previous study of a much larger group of people, very similar in every way, in Bolivar County, which joins Sunflower County, indicated that only about one-fifth of the attacks of malaria occurring in this locality were seen and treated by physicians. The treatment given in most cases that are treated by physicians is not sufficient to disinfect the patients. Those who treat themselves with chill tonics or quinine do not know it should be continued long enough to destroy all their parasites, and if they knew, quinine is not available in the necessary form nor at a price that would lead to its proper use. It may be stated, therefore, that very few cases of malaria are disinfected by treatment, and that whatever frequency of relapse is indicated in this group is not influenced to any great extent by disinfection by treatment. It is influenced, however, by treatment of the attacks, to the extent to which such treatment as they get

may influence it, for almost all persons who have acute attacks of malaria get quinine treatment in one form or another for a few days, until the active symptoms are relieved.

We have for consideration the history of 3815 persons taken from June 24, 1918, to about October 15, 1918. These histories were carefully taken by Dr. R. D. Dedwylder, who is experienced in this kind of malaria work. A test of a group of the same kind of people in Bolivar County in 1917 showed that malaria parasites were demonstrable in the blood of 54 per cent of those who thought they had malaria at the time. This indicates an accuracy of at least 54 per cent in the histories under consideration. It is probably considerably greater than that, because this estimate of accuracy is based upon a single blood examination, frequently in the case of persons who had been taking more or less quinine before the blood examination was made. This, as is well known, would lead in many instances to negative findings in persons who have malaria.

Of the 3815 persons whose histories are considered here, 1407 had attacks of malaria during 1917. Of these 533, or 37.88 per cent, had attacks also in 1918. This includes, of course, the few who may have lost their infection and later become reinfected.

Of the 2408 persons who gave negative histories for 1917, only 241, or 10 per cent, had attacks in 1918. A certain amount of infection and reinfection is taking place in such a locality where malaria is so prevalent, and this latter figure may be taken to represent the maximum amount of new infection that takes place. It is in excess of the actual amount of new infection, however, because it includes relapses in persons who had previously been infected and may have carried the infection for many months or possibly one or more years. That these are not a negligible quantity is shown by the fact that of a group of 2176 persons who claimed not to have had an attack of malaria during the previous twelve months, 18.38 per cent were found to have malaria parasites in their blood at the time. If we assume the same frequency of relapse, viz., 37.88 per cent, in this group of persons who give negative histories as to previous attacks but who have parasites in their blood, as is found to occur in those who give positive histories, we should have to deduct 6.96 per cent from the 10 per cent to get the actual new infection rate in this group.

If we assume the same proportion of reinfection in those who had attacks in 1917 as is indicated in those who did not have attacks in 1917, viz., 10 per cent, there remain 393 cases of relapse. The total number of persons who had relapses will fall somewhere, therefore, between 393 and 533, or between 50.77 per cent and 68.86 per cent, of all persons who had attacks. It is probably considerably nearer the higher figure.

Conclusions. The facts stated seem to warrant the conclusions that under the conditions named:

1. Between 27.74 per cent and 37.74 per cent of all persons who have attacks of malaria during a given year will relapse during the following year;

2. From 50.77 per cent to 68.86 per cent of all persons who have attacks of malaria during a given year have relapses and not new infections.

THE EARLY RECOGNITION OF HYDROCEPHALUS IN MENINGITIS

By Kenneth D. Blackfan, M.D., Baltimore, Md.

INTERFERENCE with absorption of the cerebrospinal fluid in acute meningitis may be brought about by an exudate which obstructs the foramen of Magendie and the foramina of Luschka, or which partially or completely blocks the cisternæ (magna, interpeduncularis, and pontis) at the base of the brain, preventing the free distribution of cerebrospinal fluid throughout the cerebral subarachnoid space. The spinal subarachnoid space may be partially or completely filled with exudate, thus limiting the participation of this surface in the absorption of the cerebrospinal fluid. Various combinations of these processes may coexist. In any event if the absorption of cerebrospinal fluid is diminished for a sufficient length of time, hydrocephalus is produced.

A brief discussion of the formation and the circulation of the cerebrospinal fluid and the more recent information concerning hydrocephalus will not be out of place here.

Cerebrospinal fluid is formed within the ventricles from the activity of the choroid plexus. Under normal conditions it passes from the ventricles through the various foramina (foramen of Magendie and foramina of Luschka) to the subarachnoid system, where it is absorbed. Absorption in the ventricular system is negligible. From the subarachnoid system the cerebrospinal fluid is absorbed directly into the blood stream. Although absorption takes place from both the cerebral and the spinal subarachnoid systems, cerebral absorption is much greater than spinal absorption. This is due to the fact that a much greater surface is concerned in the drainage and that a more extensive blood vascular area is exposed to contact with the cerebrospinal fluid. Disproportion between the formation and the absorption of cerebrospinal fluid results in its accumulation and its retention within the ventricles.

Hydrocephalus always is secondary to some process that interferes with the normal circulation or absorption of cerebrospinal

fluid. Anatomically, two types have been demonstrated—obstructive and communicating. Obstructive hydrocephalus develops because the cerebrospinal fluid cannot escape from its place of origin in the ventricles to the cerebral and spinal subarachnoid space where absorption takes place. Communicating hydrocephalus—the channels of communication between the ventricles and the spinal subarachnoid space being patent to a greater or less degree—results because the cerebrospinal fluid cannot reach the cerebral subarachnoid space, where the greater part of absorption takes place. In the majority of instances this is due to adhesions which obliterate the various cisternæ or centers from which the cerebrospinal fluid is distributed over the cortex of the brain. A combination of the two types may result, if in addition to interference with the absorption of the cerebrospinal fluid from the subarachnoid space there is an inadequate communication between the ventricular and the subarachnoid system.

The primary cause of chronic hydrocephalus in a series of cases studied recently was a previous meningitis in 14, a congenital absence of the aqueduct of Sylvius in 3, and a tumor blocking the iter in 1.

A differentiation between the two types of hydrocephalus by clinical signs alone is difficult, as the symptoms produced are essentially the same. The type of hydrocephalus may be suggested by the amount of cerebrospinal fluid that is obtained in lumbar puncture. Increase in amount of cerebrospinal fluid in acute infections of the meninges, the influence of posture on the amount of fluid, and alteration in the pressure in the cerebrospinal system have to be taken into consideration before drawing conclusions from the results of lumbar puncture alone. The two types of hydrocephalus can be differentiated, however, by the phenolsulphonephthalein test. In obstructive hydrocephalus, when injected into the ventricle, phenolsulphonephthalein does not appear in the cerebrospinal fluid obtained from the lumbar subarachnoid space within forty minutes, if at all. In normal patients and in the communicating type of hydrocephalus it appears promptly (six to twelve minutes). In communicating hydrocephalus, absorption of the dye, when injected into the lumbar subarachnoid space, is greatly diminished. Less than 20 per cent is excreted in the urine in two hours as compared to 35 per cent to 60 per cent in normal patients. In obstructive hydro-

cephalus, if the cisternæ and meninges are not affected, absorption is as prompt as in normal individuals. This phenolsulphonephthalein test has been employed in the study of a comparatively large number of patients with chronic hydrocephalus, and when properly carried out affords accurate information as to the patency of the foramina between the ventricles and the subarachnoid system and regarding the absorption from the subarachnoid space. Recently Dandy (1) has suggested that cerebrospinal fluid removed from the ventricle by ventricular puncture be replaced by air. When this is done and an *x*-ray is taken, the ventricles appear clearly outlined. By this procedure a hydrocephalus can be demonstrated and its extent measured and by the simultaneous use of the phenolsulphonephthalein test the type of hydrocephalus can be determined.

It has long been known that hydrocephalus is a frequent complication of meningitis, but until recently there has been no means by which its early recognition has been possible or a differentiation between the two types of hydrocephalus could be made, both of which are essential for successful treatment.

In the present study I have carried out the phenolsulphonephthalein test (2) in patients with meningitis in which hydrocephalus developed and in a few cases ventriculograms have been made.[1] Particular attention has been paid to the early diagnosis of hydrocephalus and to the pathological findings. Twenty-five cases of hydrocephalus were studied.

Meningitis due to the streptococcus, the staphylococcus aureus, the influenza bacillus, and the pneumococcus is a terminal manifestation in the majority of instances, secondary to a primary focus elsewhere. The entire course of the meningitis is usually of short duration, which explains the infrequency of hydrocephalus in meningitis due to these organisms. Hydrocephalus was observed, however, in the course of a meningitis due to the influenza bacillus in two patients four and eight months of age, respectively. They lived about two weeks. A communicating hydrocephalus was demonstrated at autopsy in one, and an obstructive hydrocephalus in the other. In the latter the hydrocephalus was suspected, as it was impossible to obtain more than a few drops of cerebrospinal

[1] I wish to express my indebtedness to Dr. Walter Dandy and to the staff of the *x*-ray Department for their interest in making these *x*-ray pictures.

fluid by lumbar puncture. The phenolsulphonephthalein test showed than an obstruction existed between the ventricular and the subarachnoid systems, and at autopsy the basal foramina were found to be obstructed by a thick purulent exudate.

The infrequency of hydrocephalus in tuberculous meningitis is due probably to the relatively slight involvement of the meninges. It is only occasionally that the exudate is so situated or sufficiently large in amount to interfere with the avenues of exit of the cerebrospinal fluid from the ventricles or to diminish the absorption from the subarachnoid space by involving the cisternæ at the base of the brain. In tuberculous meningitis two cases of communicating hydrocephalus were demonstrated. In each patient phenolsulphonephthalein appeared promptly in the lumbar subarachnoid space after its introduction into the lateral ventricle, but absorption from the subarachnoid space was greatly diminished. At autopsy the basal foramina were found to be patent, but absorption was limited to the spinal subarachnoid space by an exudate involving the cisternæ. In four cases the hydrocephalus was of the obstructive type. In these patients, phenolsulphonephthalein, after its injection into the ventricles, did not appear in the lumbar subarachnoid space. In these cases the foramina of exit at the base of the brain were obliterated by a tuberculous exudate.

The majority of the cases of hydrocephalus occurred in meningococcus meningitis. In 25 cases occurring in the course of acute meningitis, 17 of them were due to the meningococcus. Communicating hydrocephalus developed in 8 of the 17 cases, and in 9 the obstructive form was found. Ten of the 17 patients in this series died and 7 recovered. Two of the 7 patients had an obstructive hydrocephalus and improvement followed promptly after the introduction of antimeningococcus serum into the ventricles. In 4 patients with a communicating hydrocephalus, the process became arrested after combined intraventricular and intraspinous treatment. The patients made an uneventful recovery. One patient developed a chronic hydrocephalus (communicating). He was three months old and was first seen twenty-four hours after the onset of the meningeal symptoms. The meningococcus was grown from the blood and the cerebrospinal fluid. Antimeningococcus serum was administered intravenously and into the lumbar subarachnoid space. After the first few days the meningococci disappeared from the cerebrospinal fluid. The temperature remained irregular. The meningeal symptoms did not disappear, and from time to time, in

spite of treatment, organisms reappeared in the cerebrospinal fluid. He was treated intensively with serum injected directly into the ventricles and the lumbar subarachnoid space over a period of twenty-four days before the meningococci permanently disappeared and the cerebrospinal fluid became normal. Seven months after the onset of the meningitis the head was greatly enlarged, and a ventriculogram showed almost complete destruction of the cortex. (Fig. 1.) The patient is alive at the present writing. Autopsy was performed in the 10 fatal cases and the clinical diagnosis was confirmed by demonstration of the exciting cause of the hydrocephalus. In 7 cases (obstructive hydrocephalus) an exudate occluded the foramina at the base of the brain and in 3 cases (communicating hydrocephalus) the basal cisternæ were totally obliterated by a thick purulent exudate. Whether an exudate or adhesions are found at autopsy in this form of meningitis depends primarily on the duration of the disease.

It is not within the scope of this paper to discuss the pathological process met with in the various types of meningitis. Acute hydrocephalus in meningitis develops because, as in chronic hydrocephalus, there is a diminution in the absorption of the cerebrospinal fluid. The important point to recognize is that the lesion must be so located as to obstruct the outflow of cerebrospinal fluid from the ventricles to the subarachnoid space, or else to limit the area of absorption from the spinal or cerebral subarachnoid system. The disappearance of the exudate and the formation of adhesions determine the transition of an acute to a chronic hydrocephalus, and the re-establishment of an equilibrium between the formation of cerebrospinal fluid and its absorption determines whether the process will become arrested or progressively advance. The chronicity of meningococcus meningitis makes it the form of meningitis *par excellence* for the development of a chronic hydrocephalus. Meningitis due to other organisms almost without exception is fatal and in a short time.

TABLE I

ACUTE HYDROCEPHALUS IN MENINGITIS

TYPE OF MENINGITIS	NO. OF CASES OF MENINGITIS WITH HYDROCEPHALUS STUDIED	TYPE OF HYDROCEPHALUS	
		OBSTRUCTIVE	COMMUNICATING
Influenza bc.	2	1	1
Tubercle bc.	6	4	2
Meningococcus.	17	9	8
Total.	25	14	11

Attention may be directed to a hydrocephalus developing in meningitis by the onset of certain symptoms. The diagnosis is readily established when the condition is of long duration and the symptoms of increased intracranial pressure—headache, stupor, vomiting, enlargement of the head, and changes in the eye grounds—are present. The early manifestations of hydrocephalus, however, are so closely interwoven with the symptoms of the meningitis itself that they are often difficult to recognize. Hydrocephalus should always be suspected with the persistence of symptoms of meningeal irritation (fever, hyperesthesia, irritability, or drowsiness, rigidity of the muscles of the neck and extremities, hyperactive reflexes, tremors, etc.) or their reappearance after the symptoms of meningitis have subsided. Infants invariably have a tense and bulging fontanella and in children MacEwen's sign is positive. It should be remembered that these symptoms cannot always be referred to the hydrocephalus alone. We often see at the onset of acute meningitis and throughout the course of the disease manifestations indicative of increased intracranial pressure—headache, fever, vomiting, and muscular rigidity, which do not mean necessarily that hydrocephalus is present. I believe that much confusion has been caused by referring to such a condition as hydrocephalus. For instance, in tuberculous meningitis there is present quite constantly a marked increase in the amount of cerebrospinal fluid, but at autopsy a picture quite the reverse of that seen in hydrocephalus is found. The sulci are distended with fluid, the brain is edematous, and though there is a varying increase in the size of the ventricles, one does not find flattening of the convolutions, atrophy and compression of the brain substance, and the marked dilatation of the ventricles which characterizes the latter condition. A number of patients with tuberculous and meningococcus meningitis have been studied by determining the amount of cerebrospinal fluid withdrawn, by the phenolsulphonephthalein tests, and by the pathological findings at autopsy. In these patients there was no interference with the absorption of cerebrospinal fluid, and at autopsy the findings characteristic of hydrocephalus were not present. It is not at all likely that an increase in the amount of cerebrospinal fluid can produce other than a temporary and insignificant hydrocephalus unless there is an associated diminu-

tion in the absorption of the fluid. The results are shown in the accompanying table:

TABLE II

Case	Diagnosis	Phenolsulphonephthalein Tests		Spinal Fluid		Autopsy
		Patency of Communication	Absorption from Subarachnoid	Pressure	Amount	
1	Tbc. meningitis.	+10 minutes	Per Cent 45	Increased	40 c.c.	Ventricles not dilated, exudate slight, not involving the basal foramina or cisternæ.
2	Tbc. meningitis.	12 minutes	40	Increased	55 c.c.	do
3	Tbc. meningitis.	8 minutes	38	Increased	35 c.c.	do
4	Tbc. meningitis.	14 minutes	42	Increased	45 c.c.	do
5	Meningococcus meningitis	12 minutes	55	Increased	60 c.c.	do
6	Meningococcus meningitis	10 minutes	48	Increased	40 c.c.	do
7	Meningococcus meningitis	8 minutes	62	Increased	45 c.c.	do

Abnormal changes in the eye grounds and enlargement of the head when present are symptoms indicative of an hydrocephalus, but they seldom are seen early in its development, and so are of but little aid in making the diagnosis. This is especially true before the fontanelles are closed and the sutures firmly united. A considerable atrophy and compression of the brain take place before the intraventricular pressure becomes sufficient to cause marked changes in the eye grounds and an enlargement of the head. This is well illustrated in the case of an infant, three months of age, who was observed from the onset of an acute meningococcus meningitis, throughout the various stages of development from an acute to a chronic hydrocephalus. This is graphically shown in Table III.

The amount of cerebrospinal fluid withdrawn by lumbar puncture affords the most helpful clinical sign of hydrocephalus, although, as previously mentioned, it is not absolutely dependable. In hydrocephalus the cerebrospinal fluid is under greatly increased pressure and an abnormal amount is obtained readily or it is obtained in small amount and with difficulty.

TABLE III

Duration of Disease	Circumference of Head	Eye Grounds	x-ray of Ventricles	Phenolsulphonephthalein Tests: Patency of Communication	Phenolsulphonephthalein Tests: Absorption from Subarachnoid Space	Symptoms
Onset	44 cm.					Collapse, fever, depressed fontanella, petechiæ.
1 month	44 cm.					Bulging fontanella, rigidity, hyperesthesia.
2 months	44.0 cm.					Bulging fontanella, rigidity, opisthotonus
3 months	44.3 cm.	Slight dilatation of retinal vessels. Margin of disk clear. Normal physiological cupping.	Ventricles dilated. Marked cortical compression.	+	9 per cent	do
4 months	46.5 cm.	do	do	+	9	Opisthotonus disappeared, vomiting, tense fontanella.
7 months	49.5 cm.	do	Practically no cortex seen. Ventricles greatly enlarged.			Bulging fontanella, separation of sutures, craniotabes, rigidity, vomiting, emaciation.

A definite increase in the amount of cerebrospinal fluid of 50 c.c. or more, withdrawn repeatedly when the other signs of the acute infection of the meninges have subsided, is significant of a communicating hydrocephalus. Whilst this is suggestive evidence, in itself it is not sufficient to establish the diagnosis, as relatively large amounts of cerebrospinal fluid are sometimes found in obstructive hydrocephalus.

Small amounts of cerebrospinal fluid obtained by lumbar puncture suggest an obstructive hydrocephalus. If the subarachnoid space has been entered and the fluid is not too thick to run through the needle, it is relatively safe to conclude that there is an

FIG. 1. ROENTGENOGRAM TAKEN SEVEN MONTHS AFTER THE ONSET OF AN ACUTE ATTACK OF MENINGOCOCCUS MENINGITIS.

Phenolsulphonephthalein Test: Free Communication between the Ventricles and the Spinal Subarachnoid Space. Absorption from the Subarachnoid Space, 9 Per Cent in Two Hours. Roentgenogram shows Lateral Ventricles Markedly Dilated (*A*), and Compression of the Cortex (*D*).

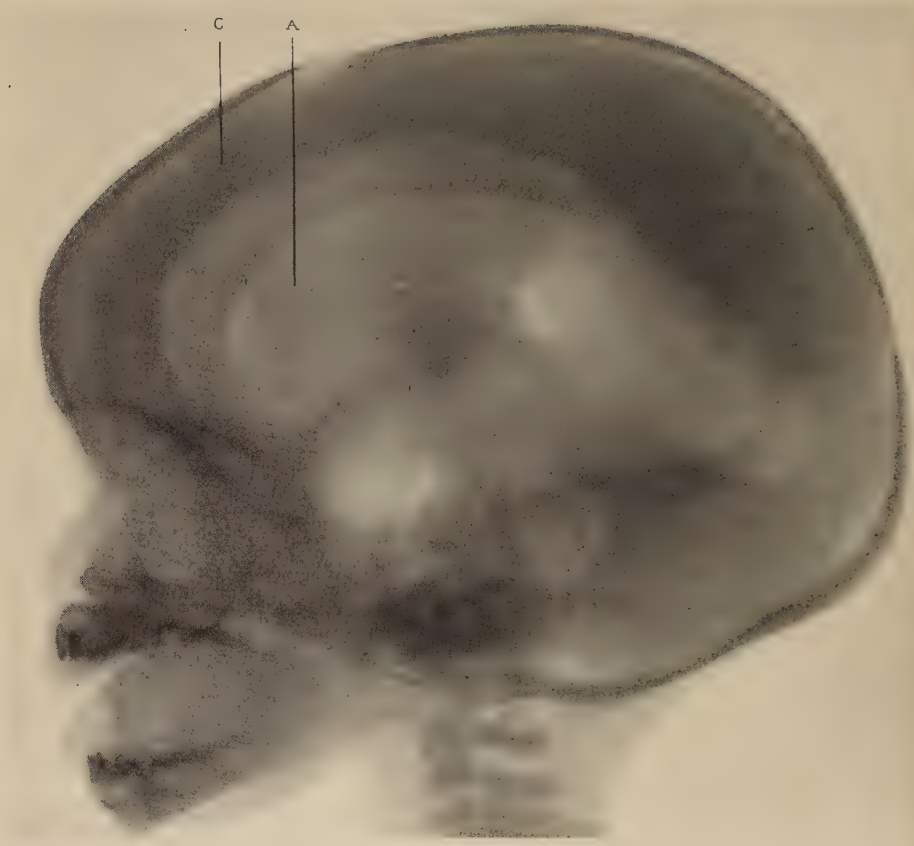

FIG. 2. OBSTRUCTIVE HYDROCEPHALUS IN A PATIENT AGED THREE MONTHS.

The Onset of the Hydrocephalus Was Suggested by the Persistence of the Symptoms of Meningitis. The Cerebrospinal Fluid Was Obtained Readily for Ten Days, and then Only a Few Drops Flowed from the Needle. Phenolsulphonephthalein Test: No Communication between the Ventricles and the Subarachnoid Space. Absorption from the Subarachnoid Space 55 Per Cent in Two Hours. Roentgenogram shows Dilated Lateral Ventricle (*A*), with Compression of the Cortex (*C*).

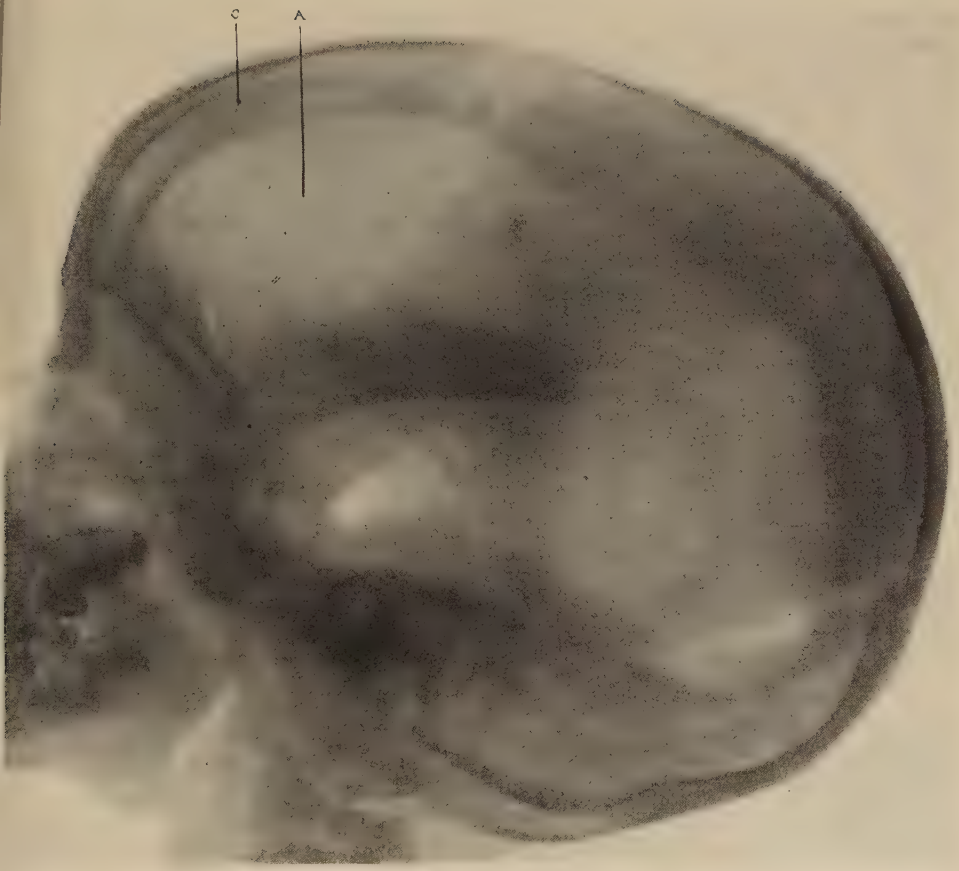

FIG. 3. COMMUNICATING HYDROCEPHALUS IN A PATIENT TWO YEARS OLD.

Untreated for Six Weeks Following the Onset of an Acute Meningococcus Meningitis. Examination Showed Rigidity of the Neck, Positive Kernig's Sign, and a Low-Grade Optic Neuritis. Phenolsulphonephthalein Test: Free Communication between the Ventricles and the Subarachnoid Space. Absorption from the Subarachnoid Space 8 Per Cent in Two Hours. Roentgen-ray examination—Dilated Ventricles (*A*), with Atrophy and Compression of the Cerebral Cortex (*C*). The Patient Died, although Antimeningococcus Serum was Administered into the Ventricles and into the Lumbar Subarachnoid Space.

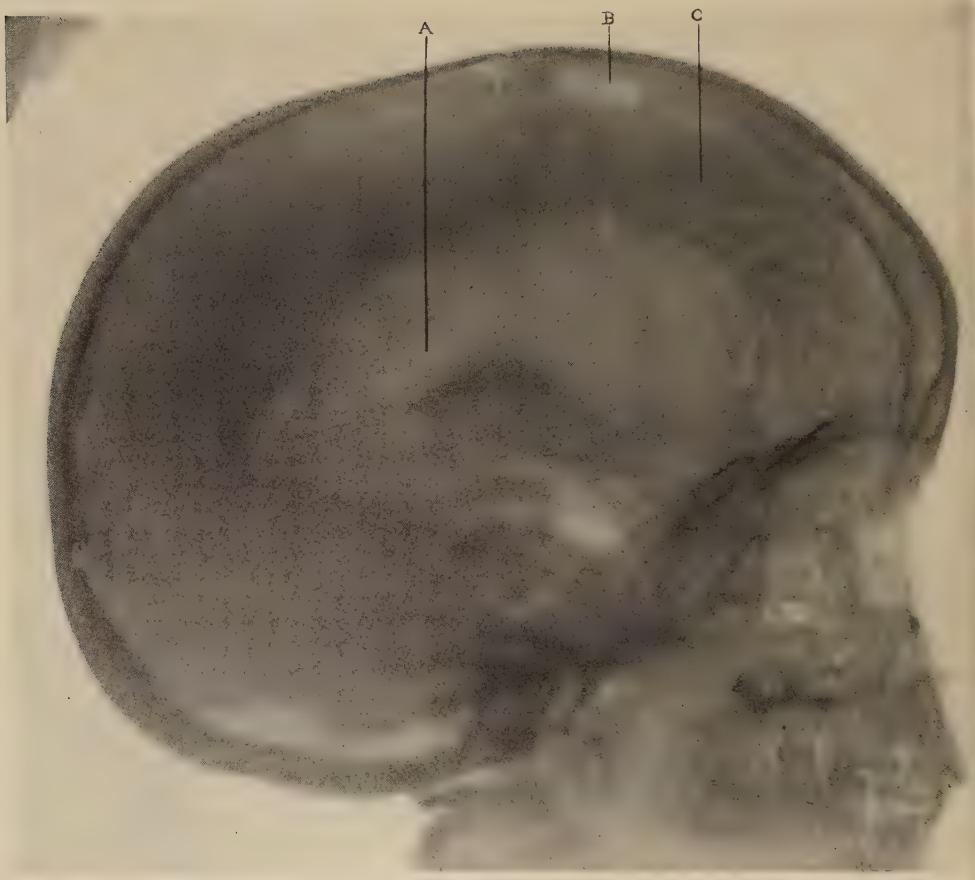

FIG. 4. THE PATIENT, AGED THREE YEARS, WAS TREATED FOR TWO WEEKS WITH ANTIMENINGOCOCCUS SERUM.

He Did Not Improve and Meningococci Persisted in the Cerebrospinal Fluid. Phenolsulphonephthalein Test: Absorption from the Subarachnoid Space was Diminished (13 Per Cent in Two Hours). Ventricular Injection of the Dye through a Trephine Opening Demonstrated a Communication between the Ventricles and the Lumbar Subarachnoid Space. The roentgenogram shows the Enlarged Lateral Ventricles (*A*), the Trephine Opening (*B*), and Compression and Atrophy of the Cerebral Cortex (*C*). After Three Injections of Antimeningococcus Serum into the Ventricles the Organisms Disappeared. The Patient Made an Uneventful Recovery.

exudate so situated as to prevent the free flow of cerebrospinal fluid from the ventricles to the spinal subarachnoid space. In obstructive hydrocephalus relatively large amounts of cerebrospinal fluid may be recovered at the first lumbar puncture, and then the quantity lessens so that only a few drops are obtained at successive punctures. (Fig. 2.) Corroborative evidence of the presence of hydrocephalus may be shown by the results from puncture of the ventricle, as in such cases the cerebrospinal fluid in the ventricles is under increased pressure and an excessive amount can be withdrawn.

The early recognition of hydrocephalus is of practical importance in meningitis, due to the meningococcus. Many cases of hydrocephalus, the result of meningococcus meningitis, are reported in the literature in which the hydrocephalus developed despite treatment with antimeningococcus serum. This has been in the majority of instances when treatment was instituted late, for the outcome at this stage of the disease even with appropriate treatment is uncertain. The earlier and the more intensive the treatment the better the chance of recovery. In obstructive hydrocephalus, if the serum is introduced only by lumbar subarachnoid injection, there is the danger of organization of the exudate and also that the meningococci remaining in the ventricles are not subjected to the influence of the serum. In this form of hydrocephalus the antimeningococcus serum should be injected directly into the ventricle as well as into the lumbar subarachnoid space. Also in communicating hydrocephalus the intraventricular injection of serum is advisable. A larger amount may be injected and thereby brought into direct contact with the exudate and in greater concentration than by the lumbar subarachnoid injection alone. (Fig. 4.)

The capacity of the meninges to absorb cerebral spinal fluid should be tested by the lumbar subarachnoid injection of phenolsulphonephthalein, when the symptoms of meningeal irritation persist or when they reappear after the vigorous use of antimeningococcus serum. A distinct diminution in the absorption of cerebrospinal fluid indicates a communicating hydrocephalus. This diagnosis can be confirmed by determining the patency of the foramina between the ventricular and the subarachnoid systems by the injection of phenolsulphonephthalein directly into the ventricle. If the symptoms are the result of an obstructive hydrocephalus alone the

absorption of the cerebrospinal fluid from the lumbar subarachnoid space will not be diminished. The diagnosis in this type of hydrocephalus will then depend on the non-appearance of phenolsulphonephthalein in the lumbar subarachnoid space after its injection into the ventricle. These tests add nothing to the severity of the treatment. They do not demand any unnecessary operative procedure, as under such circumstances it is necessary to bring serum, either through an open fontanelle or through a trephine opening, in as large an amount and as concentrated a form as possible, directly into contact with the purulent exudate at the base of the brain. At the same time, if desired, the size of the ventricles and therefore the degree of the hydrocephalus may be demonstrated by *x*-ray.

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PULMONARY STREPTOTHRICOSIS

By Norman Bridge, Washington, D. C.

SOME fifteen cases of streptothricosis of the lungs (actinomycosis) were observed by me in Los Angeles, Cal., in the space of a few years, beginning in 1907. (1) Some of the cases resembled tuberculosis in symptoms and signs, and some were mixed cases of tuberculosis and this disease—the two organisms being found in the same sputum. Such were the worst and most helpless cases. In most patients hemorrhage—usually slight—occurred at some time; but in a few instances large quantities of fetid, bloody mucopus were coughed up almost daily for weeks, the evidence of cavity being present. When blood appeared, unmixed with much serum and mucus, it usually coagulated firmly and quickly. In the uncomplicated cases fever was rarely high and emaciation not rapid.

The cases originated in many different localities, and it was impossible to say that any of them, with one possible exception, arose from a known case of the disease in man or animal. In the pure cases there was no such tendency to begin in the apex as is the rule in tuberculosis. The cases of mixed infection sooner or later all died; nor did they show, in spite of everything that could be done, any tendency to improve even temporarily. In no case was the lung lesion secondary to the disease in other parts of the body; but in one there was a skin lesion following that in the lung.

The micro-organisms were the form known as *Streptothrix actinomyces*, except that there was an absence of the so-called "clubs" so generally found in the disease in cattle. The clubs are rarely found in human lung cases; and they are not essential to the true organisms—a view held by a large number of writers, among them Bevan, Hitchins, Hodenpyl, Levy and Klemperer, Litton and Levy, Lord, Ruhräh, Stokes, Werthen and Olney, Wood and Eshner, and Wynn. A number of writers hold that neither granules nor clubs are essential—among them Ashton and Norris, Heracz, Caglieri, Chiari, Hamm, Litton and Levy, Musser and Gwyn, Scheele and Petrusky, and Weber.

The late Dr. Edith Claypole,[1] the pathologist in charge of my laboratory at the time, made extensive studies of some of these cases. Later, in the laboratories of the University of California she continued her researches into the nature of the streptothrices and their relation to the bacilli of tuberculosis. (2) Following are notes of a few of the cases in some detail. They are illustrative of the series:

Case I. The most marked example of the disease. Patient, Mr. A., a middle-west farmer of forty, came with a casual picture of rapid phthisis, but no tubercle bacilli were found—only swarms of actinomyces. He expectorated unbelievable quantities of fetid muco-pus and blood for many weeks continuously—sometimes a pint in twenty-four hours. The whole left lung was more or less involved, the upper part most. There was a little fever, moderate emaciation, and the patient was up and about most of the time. Gradually the expectoration lessened, and the man recovered after several months with a large mass of consolidation in the upper third, reduced vesicular murmur, and bronchial breathing over the whole left lung. He had continued well three years afterward.

Case VI. Mr. M., a middle-aged business man who came with a slight deposit in the right apex and a more extensive one in the lower left posteriorly. Expectoration gradually lessened, while marked fibrosis came on, and grew worse after cough and expectoration had substantially ceased. Finally the fibrosis was so extreme that the breathing was almost entirely abdominal, and dyspnea was marked on the slightest exertion. After he had apparently been well of his original lesions for several months, he went to an altitude of 5000 feet, where he was seized with some acute affection and died in a few days.

Case VII. Complicated by tuberculosis. Mr. B., aged twenty-five years, had been sick with moderate cough and purulent expectoration for over a year, when he began to cough up blood, and came under my observation. The amount of blood was small, but the lesion, which was in the left lung at the base, grew steadily worse, consolidation and finally a cavity developed. He died in three years from the first symptoms, twenty-one months after I saw him.

[1] Dr. Claypole died at Berkeley, Cal., in 1915, from typhoid fever complicated by appendicitis, after some months of close work in making typhoid vaccine for the British and French armies—as truly a sacrifice of the Great War as any soldier shot in battle. She was a daughter of the well-known geologist, the late Prof. E. W. Claypole. Beside being a woman of great character and high purposes, she was a discriminating, industrious, and wholly dependable pathologist—with a mind admirably fitted for research.

Case IX. A bachelor of twenty-eight, a street-car conductor, first seen after he had been coughing for several months. The expectoration was slight, but had frequent streaks of blood. Actinomyces were plentiful, but no tubercle bacilli. The only physical signs were slight possible dullness in the right apex, with bronchial breathing. There was no fever or emaciation for a long time. Expectoration increased, but was never over 3 ounces daily, slightly fetid, and often blood-stained. In a little over a year the tip of his nose became red and swollen, and soon broke down in ulceration at several points. The ulcers were shallow, and their secretion contained unmistakable actinomyces. They healed under local applications of tincture of iodine, and iodine internally. Some time later he had a similar lesion on one leg near the ankle, which healed after the iodine treatment.

Case X. A sheep raiser, fifty-two years old. Six months before, he had a mild case of what was called pneumonia, and was in bed only a few days. I first saw him on March 22, 1909. He was then expectorating a half-pint of pinkish muco-pus every day; had normal temperature and marked shortness of breath. Weight 15 pounds below normal. The expectoration swarmed with actinomyces. There was a large effusion in the left pleural cavity. Three days later 20 ounces of pinkish sero-pus was aspirated. This contained what appeared to be the debris of actinomyces. Six days later, the left side remaining flat, a drainage tube was inserted and 30 ounces of fluid discharged—then the expectoration decreased promptly to about one-half of the previous amount. He soon returned to his home in Wyoming, where he improved moderately. A year later he came to me, and actinomyces in fragments were still found in the discharges. Sections of ribs were removed after his return to Wyoming, with what result I never learned; nor do I know the ultimate fate of the patient.

Case XIV. A married woman of fifty, living in the house of one of the cured cases. First seen in February, 1909. Had had a gall-bladder operation some months before, with relief of symptoms. Now she had an apparent tuberculous infiltration in the right apex in front—slight fever, expectoration, and debility, but no bacilli of tuberculosis. Four months later typical actinomyces appeared; later bloody expectoration and extension of the lung lesion and more fever. Repeatedly the fever subsided on free expectoration of large quantities of actinomyces—often in clumps—with blood. There was much pain in the right chest, extreme emaciation and for several days before death expectoration of enormous quantities of malodorous pus, suggesting the bursting into the bronchi of a large cavity. She lived nearly a year after the diagnosis of streptothrix was made.

A post-mortem examination was made of this case, with the following result, as recorded by Dr. Claypole:

"In Case XIV, T., long bacilli are recorded as found in the sputum at first and later the characteristic granules of streptothrix. In all probability these bacilli, so-called, are fragmented mycelium; ultimately the fungus appeared in masses of tangled mycelia rather than in granules, but always some material of this sort was found. In about eight months a cavity appeared at the apex and the lung involvement became more extensive, especially posteriorly.

"When death occurred the emaciation was extreme. The left lung and pericardium were normal; the right was contracted and anteriorly over the third and fourth rib cartilages the parietal and visceral pleuræ were densely adherent and the bone involvement marked, explaining the neuralgia and substernal pains complained of. When the adhesions were separated the lower part of the pleural cavity was found to contain 8 ounces of most fetid pus.

"The upper lobe of the lung was mottled black and white, was almost solid in consistence, no porous structure remaining; it contained several small cavities from the size of a pea to that of a walnut. The middle lobe was dark red, spongy, with whitish spots, and anteriorly a white, honeycombed area that was adherent to the sternum for a space of some 3 inches. This was evidently the most recent involvement.

"The lower lobe was contracted, reddish, and somewhat porous. The diaphragmatic pleural surface was much thickened and resembled a pyogenic membrane. The same mycelial masses were found in this fetid pus as had been observed in the sputum. When the lung was cut into, the same granules and mycelial masses were found in the larger bronchial tubes, together with the debris of pus and epithelial cells. There was no evidence of any lymphatic involvement in any of the bronchial or other glands.

"The microscopic examination of the tissues demonstrated the growth of the fungus from the earliest stage to the mycelial masses. Sections were made from the consolidated apex, the middle lobe near the adherent portion, the intercostal tissue, the reddish lung near the base and a piece of the thickened inferior pleural surface of the lower lobe. Some sections were stained with hematoxylin and eosin, and others by the Gram-Weigert method.

"As shown in the hematoxylin-eosin mounts, the upper lobe consisted of a large amount of fibrous material, much new granulomatous tissue, but no alveoli. The bronchial tubes of varying sizes remained more or

less full of sputum, and scattered among the granulomatous tissues were giant cells, not like those accompanying tuberculosis, but small, with only from four to eight nuclei. Never was there any sign of caseation; everything was dense and compact. In the other lobes there was some vesicular structure, but the alveoli were full of desquamated epithelial and pus cells.

"Throughout the lung patches of newly formed granulomatous tissue, with its accompanying small giant cells, were of frequent occurrence, showing tissue response to some form of irritation. In places a fine fibrillar structure was plainly seen, often apparently in circular spaces, suggesting blood vessels. This was of especial interest, as will be seen from the revelations made by the application of the Gram-Weigert method to the same set of sections."

Regarding the technique of studying the streptothricosis, Dr. Claypole stated as follows:

"In the majority of cases the sputum is characteristic and of two types: (1) glairy, mucilaginous, often quite watery; (2) purulent, more or less bloody, more or less—sometimes intensely—fetid. Both types may be found sparingly or in abundance. The second type may only have a characteristic, homogeneous, pinkish color, or be deeply blood-stained; it generally has a distinctly bad odor. This odor may belong in some degree to both kinds of sputum, but especially to the purulent form. Of eight cases, not complicated with tuberculosis, three were in Class 1 and five in Class 2.

"The small granules, usually the size of a very small pinhead, can be picked out with a needle and put on a slide for examination. They are quite tough and can be washed free of debris by putting them into a small dish of water and squirting them vigorously up and down a pipette. Careful examination of many specimens before and after this treatment shows them to be absolutely unhurt by it; only the pus and epithelial cells clinging to the outside are removed.

"Under a low magnification (Reichert objective 1 and ocular 1) the yellow color is marked; to the naked eye the fungus is grayish white. The edge is always darker, even shading into brown; toward the center it grows lighter. From this light, almost homogeneous center, the characteristic radiations arise. Higher magnification (Reichert objective 7 and ocular 1) shows the center to be a mass of pale, radiating threads, the mycelium, and at the edges a mass of threads and cocci. Both mycelium and cocci may be stained with methyl blue, the former frequently being banded light and dark in segments, sometimes granular throughout.

"Culturally, the actinomyces do not grow usually on plain agar, glycerin and glucose agar, or potato (they do not seem to be more active on one than on the other of these media); if they are present, there are small whitish masses on the surface, which on removal give the characteristic appearance under the microscope. In bouillon the germs grow better.

"In this case, XIV, the point of most recent invasion is the area of the middle lobe adherent to the chest wall. This is the point at which the study logically begins. The tissue is more nearly normal than elsewhere, some exudation into the alveoli and some granulomatous cells are present. In one of the largest bronchioles full of pus cells and other elements of sputum, the most beautiful picture of the method of invasion is found. Rod-segments, staining blackish with Gram, literally swarm in one place among the pus cells. High columnar epithelial cells surround this mass of sputum. At one point their integrity is broken, and in among the cells are masses of these black rod-segments *en route* to the deeper tissues. Again they are found in the intercellular connective tissue and even to the fibrous tissue surrounding the small blood vessels. This is of especial interest in view of the fact that in older areas of infection these open spaces with walls apparently like those of vessels are found filled with mycelial threads staining the characteristic blue. The good condition, relatively speaking, of all the tissues entirely negatives the idea that this is a process of discharge into the bronchiole, rather than an invasion of it. Of course, it is a condition of self-infection, but it shows how the disease extends, and also accounts for the rather slow manner of extension, that of contiguity, not by infection through the blood-stream.

"The development of these rod-segments into the typical mycelial masses is the next point for demonstration. The earliest stage of the growth of the mycelium from the rod-segment could not be determined, the reason for this being indicated in the cultural experiments described later. In the sections of the reddish porous part of the middle lobe, rod-segments are also found in the interalveolar tissue, also small granules of the fungus. There are many granulomatous patches and in them are found areas of interlaced fibrils staining more or less deeply with Gram stain, also masses of fibrillar substance likewise staining blue. Small fragments of mycelium can be found in the exudate in the larger bronchioles over this area also. There occur in the larger bronchial tubes some sections of the tufts of the fungus; these stain deep blue and are very distinct and characteristic. Small scattered fragments of mycelium are found in many parts of the sections.

"In the upper lobe no air-space remains, fibrous and granulomatous

tissues alone are found with some blood vessels and a few bronchial tubes; in these can be seen fragments of mycelium. The response to the extreme irritation of the parasite is the formation of new tissue, and the air cells are destroyed. Apparently the excessive new formation of tissue is unfavorable to the fungoid growth; it disappears. The parasite departs, but but function of the lung is destroyed. Further invasion of new, softer tissues presumably occurs with similar results. This total lung destruction probably accounts for the marked short-windedness of most of the patients afflicted with this disease, indicated in physical signs by the so-called extreme fibrosis.

"At what point the mycelium begins to form rod-segments is at present undetermined. They may form only when conditions become unfavorable for growth in any special region, or they may be formed in small numbers at all times. The former would be the more probable, however, in view of the larger number found at the place of invasion in the most recently infected point. It is possible that the masses of mycelium, usually found in the sputum, are not capable of entering new tissues, in fact cannot cause infection; that is, that they must become rod-segments before really being dangerous to the system.

"The peculiar manner in which the rod-segments surround the small blood vessels is worthy of further study. Finding the interlaced mycelial threads apparently in blood vessels was at first very puzzling, and only after the earlier stage of the process was discovered did it seem possible that the fungus really was in the vessels.[2]

"*Summary of Case XIV.* 1. A large amount of granulomatous tissue takes the place of all air-sacs and small bronchioles in the final stage.

"2. Marked absence of caseation and very little breaking down save in a pleural cavity.

"The unexpected results obtained from the study of the tissues in this one case of primary streptothricosis of the lung make it most desirable that more should be critically examined to determine if the course of the pathological changes is always the same or if noteworthy variation occurs.

"*Cultural and Sputum Experiments.* To investigate more fully the character of the infectious agent responsible for the disease in these cases, a series of cultural experiments were made from Cases IX and XVII.

"The contaminations unavoidable in sputum and the very poor growth of the organism on solid media made it impossible to obtain pure cultures without a much longer series of experiments than time allowed.

[2] Pollack, Lohlein, and Chiari report organisms in blood vessels of lung and other tissues.

The ordinary streak and plate methods are not suitable, since the secondary forms, growing freely, cover the surface before the streptothrix is started. Consequently bouillon was chosen, and contaminating forms, chiefly staphylococci, disregarded. The small granules found in the sputum, consisting of tufts of mycelium, were carefully picked out either with a needle or pipette, washed thoroughly in repeated changes of sterile water, and then either crushed or dropped whole into the tubes which were incubated at 37.5° C. and examined daily in hanging drops and smears, the latter stained with methylen blue and by the Gram method.

"In the hanging drop the growth of the organism is beautifully shown; in the earliest stage (twelve hours) it apparently consists of a few spores, and from them two or three delicate threads of mycelium; both stained and hanging drop mounts show this clearly. During the second, third, and fourth days the small organism grows rapidly, becoming quite a mass of threads, radiating with more or less regularity from the center of growth. By the sixth day small but distinct granules can be seen in the bouillon; these are large enough to pick up and crush on slides to make smears. On agar the growth is but feeble, never in isolated masses, owing to the presence of more rapidly growing organisms, and not recognizable to the naked eye as separate masses. In hanging drops and smears it shows fragmented mycelium and rod-segments in abundance. The little tufts in the bouillon are tangled mycelium beset with many coccus-like spores, strongly Gram-positive.

"In the early stages, up to the fourth day, the mycelium proved itself to be very resistant to stains of all kinds, only a few threads becoming colored even after prolonged treatment and none if merely the usual time was allowed. Parallel observations on the hanging drops showed the fungus to be present in abundance. Finally, by the time the small tufts became visible to the naked eye, on the fourth day, the usual staining properties began to appear and by the sixth day successful operations resulted from the standard method. At no time, however, was the organism acid-fast.

"The application of the Gram stain to this organism discloses many points in the structure not shown by the ordinary stains. There is a great variation in the diameter of the different threads and as marked a difference in their staining qualities. Some are fine and hair-like, others coarse and thick. Many of the heavy ones stain a deep continuous blue, others are finely granular throughout, some segmented at regular intervals, like long strings of large bacilli, again like strings of streptococci, or in separate organism, like bacilli; the rod-segments among those that take the Gram stain in whole or part are many that show only the counter stain

and even that faintly; some are large, some small; the very young and the old degenerate threads. After becoming familiar with the organism it is easy to trace the same irregularity in staining in the tissues, though here the fragmentation is not a marked phase, save where the formation of rod-segments has occurred. The resistance to stain of the young mycelium also serves to explain the notable absence in the tissues of very young forms growing from the rod-segments. It is a well-known fact that micro-organisms in tissues are more difficult to stain than in pus, sputum, or cultures. It may be the difficulty in hardening the tissues rapidly enough to fix the organisms. In the case under consideration it would seem to be some qualities in the organisms themselves. Only as they grow old they lose the power and again fail to color typically. The exact conditions under which the rod-segments form are as yet not determined. It is evident that by no means does all mycelium fragment into them. Much of it dies, as evidenced by fine granulation and final lack of stain.

"*Summary*. 1. The fungus is found to be markedly pleomorphic, occurring in (*a*) the classical grain or tuft, in culture and tissue, (*b*) fragmentations, bacillary, or even smaller, like granules, in tissues and discharges and some culture (solid) media. Very variable in size of mycelium.

"2. The very young mycelium is resistant to all stains; the old threads likewise fail to stain.

"3. In cultures and tufts the mycelial masses always show large numbers of small Gram-positive organisms (spores). Fine branching mycelium in the very early stage starts from these structures (demonstrated in hanging drops and smears). They are negative to Moeller's method for staining spores of ordinary fission fungi. They were not demonstrated in the tissues.

"4. The active infectious agent in tissues is apparently the rod-segment.

"To extend the study somewhat further a series of preparations was made, from the sputum of many patients, tuberculous and others, as well as from Cases IX and XVII. This was to determine whether the Gram picture was diagnostic of the disease and whether it appeared in sputum in the absence of microscopic tufts. No tuberculous sputum showed the same results. In Cases IX and XVII particles of sputum chosen, carefully avoiding any macroscopic piece of the fungus, invariably gave rod-segments and fragmented mycelium. At one time when the pus appearance of the sputum was negative in Case IX the rod-segments and mycelium showed abundantly by Gram stain.

"Culture in bouillon always gave positive results in the absence of fungus in the sputum visible to the naked eye. By these two methods,

moreover—the Gram stain and bouillon culture—a case that was under observation for diagnosis was suspected and proved to be positive to culture. In a few days with severe coughing and profuse expectoration the macroscopic granules appeared, clinching the diagnosis.

"If continued observations show these two methods to be absolutely trustworthy, it will be possible to make an early and reliable diagnosis for this disease. The simplicity of a bouillon culture and hanging drop examinations, together with some Gram-stained films, brings it within the reach of all who are near any sort of laboratory facilities."

Dr. Claypole did a great amount of work on these cases, and demonstrated that the mycelial threads and rod-segments can usually be found in the sputum in the lung cases often days before "they appear in masses large enough to give the peculiar radiating appearance so characteristic of streptothrix actinomyces."

The treatment of these cases, beyond the use of tonics with rest and outdoor air, was by iodine in some form and rather full doses, and sulphate of copper in doses of $\frac{1}{4}$ to $\frac{1}{3}$ grain three or four times a day.

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A FEW OBSERVATIONS ON THE SYMPTOMATOLOGY AND ETIOLOGY OF THE ENDEMIC FORM OF TYPHUS FEVER

By Nathan E. Brill, M.D., New York

UNDER the ægis of the presidency of Sir William Osler, I had the privilege of presenting to the Section on Medicine at the Seventeenth International Medical Congress, held in London in August, 1913, a communication on "An Acute Infectious Endemic Disease, Similar to, Perhaps a Modified Form of Typhus Fever."(1)

At that time my own investigations and those of others, stimulated by my previous communications (2) on this subject, had not, to my mind, settled the identity of this disease, a reasonable doubt existing as to whether it was really typhus fever, chiefly because of the anomalous form in which it appeared. Since then the researches of my pupil, Dr. Harry Plotz (3, 4, 7), assisted by the equally brilliant labors of his collaborators Drs. Peter K. Olitsky (4, 5, 6, 8, 9, 10), Geo. Baehr (4, 7, 11, 12), and subsequently those of Dr. B. S. Denzer (5, 6, 9), and the martyr Dr. Carlos E. Husk (5, 9), have settled the identity of the disease to my mind almost beyond a doubt, even though its clinical picture differs so greatly from the typhus fever as we knew it in its classical epidemic form. Since the publication of their work, I have received letters from physicians from some of the larger cities in the temperate zones of almost the entire world's north and south latitudes, acquainting me with the fact that they had observed instances of this type of typhus fever. The latest letters are from Japan, Manchuria, and South Africa, and the last from Paris. It seemed strange to me that excepting one from London, none was received from any of the other large cities of Great Britain, the country in which typhus fever was originally studied and whose investigators gave the disease its place in nosology. This silence was most likely due to the demands on the medical profession in Great Britain incident to the Great War. Hence to recall the attention

of your countrymen to this subject, in which I know that you are particularly interested, seemed to me to be an appropriate contribution to this volume, which is dedicated to you, to whom the medical profession of the entire English-speaking world owes so much—to you, master, teacher, friend.

Typhus fever, it should be remembered, occurs in two forms, the epidemic and the endemic. If one wishes to form a true conception of the characters of the endemic form of typhus fever it would be wise to forget the clinical picture of the epidemic form as it is portrayed in monographs, text books, and systems of medicine; it would be equally wise for those with the same object in view who have *seen* epidemic typhus fever and who are familiar with its clinical features to forget the picture, because the epidemic form has only a very remote, if any, definite resemblance to the form with which they are familiar. The differences in the clinical characters between the two forms are as great as are the differences between the clinical features of a variola and a varioloid—the one familiar with the first and who has not seen an instance of the other would fail to recognize its nature on casually meeting the modified form of the disease.

Endemic typhus fever often begins with a distinct chill, though not uncommonly with a chilly sensation, followed quickly by generally distributed muscular pains and a headache. Fever immediately appears and quickly rises to its height within three or four days. The headache increases in intensity and becomes most violent, suggesting in its severity that of a meningitis. With the headache and the fever the patient becomes somewhat prostrated and in most instances is compelled to take to bed on account of the fever, of the feeling of sickness, and because muscular effort increases the severe pains in the head. After taking to bed, which may be delayed to the fourth, fifth, sixth, or even seventh day, the patient becomes somewhat apathetic, taking little interest in his surroundings or in his condition. He resents being disturbed in any way, because he knows that any body movement increases the pain in the head. The fever, as indicated by the thermometer, rises steadily from the onset until the third or fourth day of the disease, when the fastigium may be reached—occasionally the second day of the disease will show the high point of the fever. The temperature, after its initial rapidly progressing elevation, remains stationary as to morning remissions

and evening exacerbations, the difference between the two being rarely more than 1° to 1.5°, common temperature being 102° F. in the morning and 103° F. in the afternoon, sometimes 104° in the latter. Thus the fever remains, as does the headache, with persistency throughout the course of the disease, though unlike the course of the headache in the epidemic form, which disappears at the end of the first week to give place to the symptoms and signs of grave implication of the nervous system. While the patient is more or less apathetic and resents being disturbed, he sleeps a good deal, though he is rarely, if ever, stuporous. He is easily aroused, usually knows his surroundings and the time of the day or the day of the week, even though a good part of the time is passed in sleep. The sensorium, as a rule, is not much affected. Very occasionally in a toxemic patient with hyperpyrexia will a quiet delirium be observed to occur at night and to take the form of a muttering during sleep.

On the fifth or sixth day, dating from the chill, an eruption appears. This may consist of a few scattered spots not exceeding twenty in number, or of a more generous and numerous distribution amounting to many hundred, first appearing on the back and abdomen, rapidly followed by their presence elsewhere on the trunk and extremities. Occasionally the eruption will be found to appear also on the palms and soles and along the sides of the face and neck. Rarely, it occurs on the soft palate. It is the eruption which for the most part indicates the disease and establishes its identity. It begins as small, 2 to 3 mm., discrete, maculo-papular, irregularly oval spots, whose elevation is very slight, even less than 0.5 mm., of a dull dirty-pink color with indistinct outlines; in fact the outline of the spots cannot always be determined, as many of them seem to merge insensibly into the surrounding unaffected skin. The spots when pressed upon lose their color and partially their contour, but do not disappear, as may readily be seen with the use of a glass slide, under whose pressure the varying phases of color change may be evoked and demonstrated. While the spots fade under pressure, a spot shows, when thus compressed, as a dirty, pale brownish-yellow stain, which can always be identified as marking the site of the compressed spot. The spots cannot be entirely obliterated by pressure; when it is removed the spots immediately return to their original size, shape, and color.

While the eruption would thus come under the classification of an erythema, it is very rarely truly petechial. Less than 2 per cent of the spots will show a central punctate hemorrhage, giving the spots involved a distinctly pin-point, purplish center which no degree of pressure can cause even to fade. The eruption which occurs in the endemic form of the disease corresponds with what is usually termed the first stage of the eruption in classical epidemic typhus. The eruption does not go beyond this first stage, except in the rare instances just mentioned. It does not deepen in color during the progress of the disease as it does in epidemic typhus fever, but retains its dusky, dirty-pink hue throughout. These characters constitute the chief differences between the types of eruption in the endemic and epidemic forms of the disease.

When petechiæ are present they are very sparingly scattered among the otherwise abundant erythematous eruption. The eruption appears almost synchronously over all the parts of the skin, and shows no tendency to develop in crops, nor for additional spots to become apparent from day to day. When the eruption appears, it remains until the course of the infection is terminated. Occasionally the spots will begin to fade a few hours or a day before the critical fall in the temperature, on the twelfth or thirteenth day of the disease. There is very little difference between the individual spots, excepting a slight one in size and in depth of color; occasionally two adjacent spots may coalesce. The number of spots seems to depend upon the intensity of the infection—the more severe the attack the more extensive is the eruption. As a rule the eruption is composed of several hundred spots, far fewer, however, than in measles, with which the individual spots have a superficial resemblance. No group coalescence such as occurs in measles takes place in the eruption of endemic typhus fever. While the spots may be considered rubeloid, they are morbilliform rather than roseolar; in fact they ought not to be confounded with the distinctively roseolar eruption of typhoid fever. There is less difficulty in differentiating them from the eruption of the latter disease than from that of measles.

As the disease progresses the headache, fever, and eruption remain. The fever rarely rises so high as to disturb the activity of the heart action—one does not see the small, rapid, feeble pulse which commonly accompanies the myocardial degeneration induced by

the toxemia of the epidemic form. As a rule the pulse rate is not rapid, its usual range throughout the disease being between 80 and 100 beats per minute; very seldom toward the end of the disease will the rate reach 120. The blood pressure shows a tendency to become lowered as the disease advances. The pulse is commonly full, soft, and easily compressible. Occasionally dichrotism may be observed.

The face is sometimes flushed, the eyes suffused and dull; the forehead is commonly wrinkled, and many patients moan and give facial expression to the pain in their head. The tongue is commonly moist, though furred; occasionally a dry white fur covers its dorsum, with edges distinctly moist; it rarely becomes dry, as it does in the epidemic variety. The appetite is practically lost, though food is not entirely refused by the patients; they prefer nourishing fluids to soft articles of food as a rule. There are no intestinal symptoms; very seldom is tympanites noted, though constipation is common; nausea is sometimes present, and occasionally an attack of vomiting ushers in the disease. The spleen is often enlarged, being palpable in over 50 per cent of all the cases; it is often felt with its soft edge and body even as low as 4 cm. below the left costal margin. As a rule the increase in its size is not very pronounced, though sufficient to make it readily palpable.

The urine generally is concentrated and scanty, with high color, though clear. Occasionally only is albumin present and very rarely are casts observed; the last when present are of the granular variety. The albumin and casts disappear with the onset of convalescence unless a pre-existing nephritis obtains; the urine in about 40 per cent of all the cases gives a positive reaction to Ehrlich's diazo test.

The blood of patients with endemic typhus shows no evidence of reactive bone-marrow involvement. As a rule which was deduced from blood counts taken in all of our cases, the average white blood count is 10,250; the largest number of cases showed counts extending between 8000 and 14,000. Leucopenia is very rare. The normal relationship of polymorphonuclear cells to the lymphocytes is preserved; the red blood cells do not seem to be structurally affected, nor is their number, as determined by count, apparently diminished, either at the beginning, during the course, or after defervescence of the disease; this may also be equally truly said of the hemoglobin

content of the red blood cells, though a slight hemoglobinemia is observed during convalescence.

After the fever has persisted in an unvarying course for twelve to thirteen days, the temperature, as a rule, suddenly falls, and within twelve hours it returns to the normal. The fall is usually sudden, and with it the clinical signs of the disease disappear almost as suddenly as the disappearance of the fever; the headache vanishes, the expression of pain on the face is replaced by one of comfort and relief, the eruption fades, and within two days has absolutely vanished, the patient becomes alive to his surroundings, his desire for food becomes usually acute, and an appearance of health replaces that of illness. Occasionally an increased rise in the temperature to a higher point than it had reached in the course of the disease immediately precedes (precritical rise) the sudden return of the temperature to the normal. Sometimes also the return to normal takes place by descending steps in the temperature curve—(resolution by lysis), though I have never seen a lytical fall of the temperature take more than sixty hours before the course of the disease was terminated.

The disease has practically no mortality. Only one death in over 500 cases of the series studied has occurred.

Bacteriology. It was the search for the etiological factor of the endemic form of this disease which revealed definitely and absolutely that this was really a form of typhus fever. This had been suspected by me for many years, a suspicion which was subsequently corroborated by the belief of Dr. Louria (13) of Brooklyn, N. Y., and of Dr. G. A. Friedman (14) of New York City, both of whom had seen instances of this type while practicing in Russia, a country in which typhus fever is constantly present. Blood cultures had been made by our pathological department almost entirely aerobically on almost all the cases under my observation at Mount Sinai Hospital, a few having been attempted with anaerobic methods, all with negative results. Injection of infected human blood into monkeys had also been done without inducing in the animals the disease reaction. Anderson and Goldberger (15), who had been busying themselves in a study of typhus fever in Mexico, were given the opportunity of studying the blood of some of my patients in the active stage of the disease. Out of four monkeys injected by them with

blood from these patients, three showed no reaction; they did succeed, however, in getting a reaction in the fourth, from which monkey they were able to transmit the infection through numerous generations. They found such monkeys to be immune to the injection of infected blood taken from cases of Mexican typhus, and, vice versa, monkeys injected with infected blood of Mexican typhus were immune to the injection of the infected blood of the endemic form existing in New York, from which they concluded that the two diseases were one and the same, because there was a cross immunity existing between them, in my opinion with insufficient evidence. It should be said here that monkeys possess a great natural immunity against infection with typhus blood, 20 per cent only being susceptible, a circumstance which we now know accounted for our experimental failure. It had been known for some time that human blood contained the infectious agent of typhus fever ever since Moczutkowski (16) reported that he had inoculated himself with infected human typhus blood and after an incubation period of eighteen days had developed the disease. This method of inducing the disease was subsequently confirmed in human experiments by Otero (17), in Mexico. It was also known through the work of Nicolle (18), the first who successfully used animals (monkeys) to show that the disease could be transmitted to them by the injection of typhus-infected blood, through the work of Ricketts and Wilder (19), of Anderson and Goldberger (15) and of Gavino and Girard (20), that a filter arrested the passage of the infectious agent in the blood. With this knowledge presented to him, Dr. Harry Plotz conceived the idea of making a more intensive series of cultures of infectious blood with anaerobic methods, for which undertaking he qualified himself by a course in cultural methods with Noguchi at the Rockefeller Institute, using at first the latter's methods for cultivating the spirochætæ, employing ascitic fluid, kidney tissue, and liquid petrolatum as the culture medium. By this method he succeeded in getting a growth of an organism in five out of six of our cases. Subsequently the method employed was a modified Liborius-Veillon (21), using serum glucose agar instead of glucose agar in the medium.

The organism which Plotz (3) recovered from these cases had a morphological resemblance to the bacillus seen in blood smears by

Ricketts and Wilder in their earliest investigations in Mexico, though no other proof exists that the organism isolated by Plotz is the same as that seen in smears by the others. The organism thus isolated appeared in the culture tubes usually late, the limits being between three and sixteen days of incubating, as colonies, generally in the lower part of the culture medium in the tubes, never near the top. The colonies appear as round opaque spots, whose diameter varies from 1 to 6 mm. Examination of these colonies shows that they consist of bacilli, small, pleomorphic, as a rule Gram-positive, non-motile, non-acid fast, which have no capsule. The bacillus is an obligatory anaerobic organism. Its length varies between 0.9 and 1.93 microms, its width being one-fifth to three-fifths of its length. The organisms are ordinarily straight; occasionally slightly curved forms may be noted among them. Coccoid forms are likewise occasionally seen. The organism has rounded or dull pointed ends. After subcultures or transplants, degeneration and involution forms appear which differ considerably in morphology from the organisms of the original culture. Spores are not produced; polar bodies are occasionally demonstrable at one or both ends. At the same time during which these investigations were going on, Plotz (4) had the opportunity of cultivating blood from some patients with classical epidemic typhus fever who had just migrated from the Balkans, and had been held up on account of this disease by the Health Officer of the Port of New York. He was delighted to find that the organism recovered from their blood (seven positive results in seven cases) showed the identical characteristics and reactions as did that isolated from our endemic cases. From an eighth case blood was injected into two guinea-pigs, who developed a smart reaction, at whose height blood removed and cultured from their heart chambers by puncture showed the identical organism.

Plotz later obtained positive blood cultures in 50 per cent of the endemic cases, or in eighteen out of thirty-four cases of this form of the disease. The blood was taken before the crisis in all these cases. He demonstrated that the infectivity of the blood dies out shortly after the crisis, though it is still infective as long as thirty-two hours thereafter. Blood cultures taken thereafter were negative.

In a similar manner he isolated, by blood culture from a monkey and eight guinea-pigs in which the disease had been experimentally

produced, colonies with identical characteristics as those cultured from the blood of endemic and epidemic cases of the disease, thus proving the identity of endemic typhus fever, epidemic typhus fever, and experimental typhus fever. This furnished the first positive proof that the disease described by me was without doubt a form of typhus fever and satisfied me completely as to its identity.

Equally as important as was the isolation of the infective organism of the disease were the results of the serological studies made by Dr. Peter K. Olitsky (4), one of the collaborators with Plotz during the study of the etiology of the typhus fever. He found in the blood of typhus patients the presence of complement-fixing antibodies. Their presence was most marked, not in the course of the disease, but at and more particularly after the crisis, reaching their maximal concentration between the second and twelfth day after the end of the disease. These antibodies, he demonstrated, may persist for over three months.

Further, an agglutinogen from epidemic typhus gave clumping with endemic typhus serum as well as with serum from an epidemic case of the disease, and an endemic typhus fever agglutinogen gave a positive agglutination with serum taken from both the epidemic and endemic cases. He further showed that the maximal concentration of agglutinogens occurred in both forms about four days after the crisis, and that they persisted and could be demonstrated in some cases at least five months after the termination of the disease.

Similarly Olitsky proved that specific precipitin, while absent from the serum in the height of the disease, is readily demonstrated to be present at the crisis and increases in concentration with each day for a period of a week at least thereafter. Bacteriolysins and bacteriocidins against the typhus bacillus could not be determined by him in immune serum. He believes that immune opsonins are also present.

From his investigations Olitsky was enabled to draw the conclusion "that from a serological viewpoint, both these types, the organism obtained from endemic and the one from epidemic typhus fever, are two strains of the same bacterium." He got identical results from a study of experimentally induced typhus in monkeys, thus further strengthening the position that the true infective agent of the disease had been isolated.

It remained for Dr. Geo. Baehr (4), the third member of this investigating group of co-workers, to show that he could recover from a culture of the blood of animals (monkeys and guinea pigs) in whom the disease had been induced by inoculation of infective typhus blood the same organism. He also showed that the bacilli isolated from cases of epidemic typhus fever could reproduce the disease when inoculated into animals, and that at the height of the disease thus experimentally induced, the identical organism could be recovered from their circulatory blood; and that only blood which contains a sufficient number of these bacilli is infective to the experimental animal, thereby completing with them the proof that both forms of typhus fever are due to the presence of the *Bacillus typhi exanthematici.*

I am so well acquainted with their work, having watched it in its course and progress, that I do not hesitate to accept their conclusions. To my mind the proof is almost complete, there being one important link in the otherwise complete chain of evidence which is missing, namely, that no proof is established that immunity has been produced against typhus infection by the disease experimentally induced by the injection of the bacillus typhi exanthematici. What seems to me the strongest element of the truth of their work is the fact, generally accepted as a biological law, that the presence of specific antibodies in the host furnishes the strongest proof of specificity.

Since the publication of this work confirmatory studies as to the presence of the bacillus typhi exanthematici have been recorded by Popoff (22) in Serbia, by Mühlens and Ficker (24) working in Serbia, by Paneth (23) in Volhynia, and by Olitsky, Denzer, and Husk in Mexico. Baehr and Plotz, likewise working in the Balkans and in Russia, 1915–1916, recovered the identical organism from the typhus patients in those countries as they had in the local cases.

Inasmuch as it had been shown by numerous observers that the *Pediculus vestimenti* is the intermediary host of the infective agent, and that typhus fever is transmitted by the bile of the typhus-infected louse, Olitsky, Denzer, and Husk (5, 9) isolated in the typhus-infected lice of Mexico, likewise, the same organism which was found in human typhus blood, and were able to culture the organism from the lice-infected bodies; these organisms, when injected into

guinea pigs, produced the same type of reaction with the same clinical course as was produced by the injection of human typhus-infected blood. It may, therefore, be accepted as a fact that the typhus bacillus has been isolated from typhus-infected lice, and that "in its earliest stage of growth such organisms are pathogenic for guinea pigs." While the proof is most convincing that typhus fever is conveyed by the bite of typhus-infected body lice, it is still a question whether that is the only agency concerned in its transmission. In a most recent discussion at a "Typhus Congress" (25) held in the City of Mexico in January, 1919, one of the subjects which gave rise to an animated difference of opinion was that of the transmission of this disease by lice as the sole cause for the spread of the disease; some claimed that its equal prevalence among the better classes and the wealthy, where cleanliness was observed, diminished the probability of its transmission by lice alone. In previous communications, when discussing the etiology of the endemic form, I raised the same question because of certain epidemiological and biological considerations, a little less than 70 per cent of all the endemic cases occur in New York in the hot summer months, including July, August, September, and October; the fewest cases occur in the winter months of December, January, February, and March. This is the exact reverse of the conditions which obtain with epidemic typhus fever. Furthermore, it is well known that heat destroys the activity of the body louse. That it cannot live in sustained warm temperatures was demonstrated by Anderson and Goldberger, who found that they could not keep lice alive in retainers even when exposed to the warmth of their pockets, and who further showed that a sustained temperature of more than 20° C. was sufficient to cause the death of this parasite. Another factor which would suggest that the body louse may have but little to do with the transmission of the endemic form of the disease is the almost total absence of family infections. In over 500 cases which have been observed in Mount Sinai Hospital, in only two instances was another member of the family affected with the disease at the same or nearly the same time. The transmissibility of the endemic form is therefore practically *nil*. Were the body louse the sole agency of transmitting this form of the disease, husband should infect wife or wife the husband, in more numerous instances. Possibly the

attenuated virulence of the organism of the endemic form may explain this lack of transmission in families; it may also explain the relatively few instances of the disease among the poor classes of large cities with whom body lice are of common occurrence.

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THE OCCURRENCE OF TUBERCLE BACILLI OUTSIDE THE BODY IN A SANATORIUM AND HEALTH RESORT

By Lawrason Brown and S. A. Petroff, Trudeau, N. Y.

MUCH and little is known up to this time of the etiology of pulmonary tuberculosis. It is of considerable interest in all etiological work to see how much rests upon the authority of recognized workers, for it is clear to everyone that some of their premises have been based on questionable evidence and an illogical induction drawn. The widespread prevalence of the disease, clinical and occult, has led many to hold that tubercle bacilli are broadly disseminated in the haunts of the most civilized nations. The rarity of its occurrence among workers in tuberculosis sanatoria has long aroused attention and speculation. The results of an attempt to find the tubercle bacilli outside the body in the Trudeau Sanatorium and in Saranac Lake, where tuberculosis among the workers and inhabitants claims remarkably few victims, are detailed in this paper.

If we follow a patient throughout his daily routine and try to conceive where tubercle bacilli could, after escape from his body, find temporary lodgment before entry into a new host, we might discover, we thought, some difference between the occurrence of tubercle bacilli in a health center and in an ordinary city. When the patient arises at Trudeau he almost immediately goes to the bathroom to perform his toilet. There he is likely to cough, owing to the exertion of bathing or sponging, and for this reason often unable to cover his mouth when he does cough. His toothbrush used at this time must, it cannot be denied, become infected. After dressing he eats breakfast, and *a priori* it would seem likely that those eating utensils which come in contact with his lips would become infected. We refer to the spoons, forks, glasses, and cups. At meals involuntary or unexpected cough leads to the covering of the mouth with the napkin or perchance the hand. These would naturally, it seems,

become infected. During the day explosive or paroxysmal cough would produce similar infection of the hands and in all probability of the clothing and rugs. It is also conceivable that in handling objects or in shaking hands bacilli might be passed on. This, of course, would apply to books, door knobs, piano and typewriter keys, billiard cues, etc. Direct contact with the lips by kissing would, it must be assumed, lead to infection of the object kissed. The occurrence of cough while using the telephone would subject the mouthpiece to infection. Many infectious droplets must eventually reach the floor, and it seems certain that rugs and carpets would receive their quota of tubercle bacilli.

It has been conclusively proved that the feces of practically all patients with tubercle bacilli in the sputum contain tubercle bacilli. The feces and the objects they soil—the hands, the toilet bowls, and bed pans—hence become infected. The urine may also contain tubercle bacilli and may be a source of contamination. Infected milk or food was not deemed necessary for consideration in this paper.

When the patient is in bed his chances for spreading tubercle bacilli are naturally confined to the rooms in which he lives. The bedclothing, the bed, the bed table, the chair, the walls, the floors, all seem certain to be infected at times. This holds true of the bathroom as well. It is taken for granted that clothes, papers, or handkerchiefs used to cover the mouth and wipe the lips are frequently and continuously contaminated with tubercle bacilli.

It has been impossible at this time to deal with many of the points mentioned in this summary, but we hope from time to time to extend our work and eventually to cover all the points. It has seemed wise to publish the results of our experiments so far completed in the hope that others may perhaps be stimulated to pursue work along such lines and help to draw out of the tangled maze a true conception of some of the etiological factors of tuberculosis.

Many years ago Hance found tubercle bacilli in the dust from the floor of a cottage in Trudeau upon which a patient had been reported for spitting. From time to time since then casual investigations have been made of the dust in various places in the institution. For instance, the dust obtained from a large rug in the general assembly room was inoculated into several guinea pigs with negative results

concerning tuberculosis. Several years later dust was collected from one of the rooms in the Infirmary, occupied by a patient with a violent explosive cough, who rarely covered his mouth, and inoculated into a guinea pig, which remained free from tuberculosis. This led us, of course, to be skeptical about the presence of tubercle bacilli in the dust about the buildings, but we determined to make another effort to find, if possible, any lurking tubercle bacilli. The rooms selected were those occupied by patients with numerous tubercle bacilli in their sputum. The technique was as follows:

Dust Experiment, February 9, 1916. The dust from the rooms, before the daily cleaning, was collected by swabbing with sterile swabs the corners of the room, bed frames, bed tables and walls near the patients. These swabs were washed in sterile broth. The washings were treated with normal NaOH, incubated for one-half hour, then neutralized with normal HCl, centrifugalized and the sediment divided into three portions. One portion was inoculated into gentian violet media, another was examined by direct microscopic method, and the third inoculated into guinea pigs, using two for each swab. The rooms of four patients were studied. Two guinea pigs were inoculated subcutaneously in the inguinal region with the washings from the swab from the bed frame and two each for those from the bed table and walls (corners). In all twenty-four guinea pigs were used.

The gentian violet media were all contaminated mostly with molds, so a further study by this method was abandoned. All slides used to demonstrate the tubercle bacilli by direct staining methods were negative and not very satisfactory, so we decided hereafter for the dust experiments to adhere entirely to animal inoculation.

Forty-one days after the inoculation (March 22, 1916), all twenty-four guinea pigs were killed. Microscopic examination of the organs appeared to be normal, but bronchial glands were enlarged, and in a few cases the spleen was also enlarged. The suspected organs were macerated and inoculated into the second series of guinea pigs with the following result.

April 27, 1916, all of the animals in the second series were killed. Autopsies negative.

As all these results were negative we thought perhaps that our failure was due to the fact that such great cleanliness was practiced at Trudeau that no tubercle bacilli could escape mop or cloth. Hence we collected dust in two rooms in Saranac Lake Village, both occupied by patients long since dead. One of these was a very ill young colored woman and a

second a woman with a violent cough. Here again the results which followed were negative.

The mouthpieces of the telephones in common use by the patients at Trudeau were also investigated and found to contain no tubercle bacilli.

It occurred to us that infection by inhalation might be more effective than by inoculation, and a specially constructed glass box was attached to a vacuum cleaning apparatus and guinea pigs subjected to the dust from the room for one-half hour. Three guinea pigs were used and none developed tuberculosis. The results:

August 7th, three guinea pigs were subjected to dust from the rooms.

September 20, 1916, intracutaneous test of ½ c.c. of 1 per cent of O. T. without reaction.

September 24, 1916, the three guinea pigs were killed. Autopsies showed no tuberculosis. Some of the inguinal and bronchial glands, and portions of the spleen, were macerated with sterile salt solution and inoculated into a second series of three guinea pigs.

November 20, 1916, all guinea pigs in this second series were killed, and autopsies showed no tuberculosis.

Utensil Experiment. Having been unable to find tubercle bacilli in the dust, we next began the study of table utensils, especially those that come in contact with the lips. The plates, cups, glasses (water and milk), forks, spoons, and knives used by two patients who had numerous tubercle bacilli in the sputum (Gaffky VII and IV) were taken immediately after breakfast to the laboratory. It was deemed wise to group the utensils as follows: Plates and knives, cups and glasses, and spoons and forks. Particular attention was paid to those parts of the cups and glasses that come in contact with the lips.

The technique for the swabs used here was similar to that usually employed, viz., rinsing in sterile salt solution, incubation with normal NaOH, neutralization with normal HCl, and centrifugalization at high speed for fifteen minutes. The sediment was used for inoculation into two guinea pigs and studied microscopically. The details are in Table I.

For each patient we studied, one plate, one cup, two glasses (water and milk), one fork, two spoons, and one knife. To confirm the autopsies in each case a small portion of the spleen and also the pus from the glands were triturated and smears made, and in each case the acid-fast organism demonstrated in the preparation. The results showed that the spoon, forks, glasses, and cups were contaminated with tubercle bacilli, while the knives and plates remained free. Attention should be called to the fact that ordinary washing and rinsing in very hot water is sufficient to sterilize these utensils which has been proved by Price. (1)

TABLE I

	No.	Utensils	Microscopic Examination for Acid-fast Bac.	Result of Animal Inoculation Inoculated, April 26, 1916 Killed, June 6, 1916
Patient No. 1, Miss E.	U-1	Plates and Knives	Negative	*a.* No tuberculosis.
				b. No tuberculosis.
	U-2	Cups and Glasses	Positive	*a.* Moderate tuberculosis.
				b. Generalized tuberculosis.
	U-3	Spoons and Forks	Positive	*a.* Died May 1, 1916. Unknown cause (no tuberculosis).
				b. Generalized tuberculosis.
Patient No. 2, Mr. M.	U-4	Plates and Knives	Negative	*a.* No tuberculosis.
				b. No tuberculosis.
	U-5	Cups and Glasses	Positive	*a.* No tuberculosis.
				b. Questionable tuberculosis.
	U-6	Spoons and Forks	Negative	*a.* No tuberculosis.
				b. No tuberculosis.

Transmission of Tubercle Bacilli by Shaking Hands. Two patients were chosen who had large quantities of sputum with numerous tubercle bacilli. They were instructed to cough hard and frequently upon their hands, which were then washed in a small quantity of sterile water. The entire volume of the water was inoculated into guinea pigs, two for each patient. Autopsy revealed generalized tuberculosis in every guinea pig. This confirmed the previous work of Baldwin. (2)

September 1, 1916, two guinea pigs were used for each experiment and were inoculated with the washings above mentioned.

C 1*a*
C 1*b*
C 2*a*
C 2*b*

} All the washing was inoculated in the inguinal region.

October 20, 1916, the above four guinea pigs were killed and autopsy revealed generalized tuberculosis in all guinea pigs. This suggested the possibility of the transmission of tubercle bacilli to a second person by shaking hands.

After the hands had been washed again and dried, the patients once more coughed into the hands and immediately shook hands with a second person. The hands of this second person were washed as previously described and the entire wash water was again inoculated into four guinea

pigs. All of these guinea pigs remained free from tuberculosis. The details:

September 1, 1916.

C 3*a*, C 3*b*, C 4*a*, C 4*b* } Inoculated subcutaneously in inguinal region.

October 20, 1916, the four guinea pigs were killed and autopsy revealed no tuberculosis.

Saliva Experiments. Two patients with profuse expectoration containing numerous tubercle bacilli were instructed to expectorate saliva into a sterile container just before they coughed. Their saliva was inoculated into two guinea pigs, both of which developed extensive tuberculosis. The details:

September 1, 1916.

S-1, S-2 } Inoculated with saliva subcutaneously.

October 20, 1916, guinea pigs were killed and showed extensive tuberculosis.

Kissing Experiments. As the lips are soiled frequently by the sputum and always by saliva, we attempted to recover tubercle bacilli from sterile dishes which patients with sputum containing tubercle bacilli had kissed. A patient with numerous tubercle bacilli in the sputum (Gaffky VIII) was instructed to kiss a sterile Petri dish which was washed with sterile saline solution. The guinea pigs inoculated with the washings of dishes kissed immediately after the patient had expectorated and again ten minutes later all developed generalized tuberculosis, while those inoculated from dishes kissed twenty minutes after expectoration remained free from tuberculosis.

The details are below:

September 7, 1916, two guinea pigs were inoculated immediately after expectoration (K 1-*a*, 1-*b*).

Two guinea pigs were inoculated ten minutes after coughing (K 2-*a*, 2-*b*).

Two guinea pigs were inoculated twenty minutes after coughing (K 3-*a*, 3-*b*).

October 20, 1916, all guinea pigs were killed, autopsy:

K 1-*a* and K 1-*b*, generalized tuberculosis.

K 2-*a* and K 2-*b*, generalized tuberculosis.

K 3-*a* and K 3-*b*, no tuberculosis.

It was decided to investigate more closely the question of the time of day when the kissing was performed, in order to see if the infectiousness

varied. Accordingly, a patient with numerous tubercle bacilli in the sputum (Gaffky VIII) was instructed to kiss sterile Petri dishes at 7, 9 and 11 A.M., 2, 4, 6 and 9:30 P.M., and to return immediately the dishes to the laboratory. Those kissed at 11 A.M., 4, 6 and 9:30 P.M. were negative. The experiment was repeated with a patient whose sputum had few tubercle bacilli (Gaffky IV to VII) and only at 7 A.M. was the plate found positive. The details follow: (See Table II.)

Transmission of Tubercle Bacilli by Flies. It has been definitely proved that flies which have fed upon tuberculous sputum deposit tubercle bacilli in their excreta (fly specks). To verify this, however, three flies were put into a large sterile beaker and allowed to feed for three days on sputum containing large quantities of tubercle bacilli. The flies developed what appeared to be diarrhea, and deposited soft white specks forming large circles, which examination proved to contain tubercle bacilli.

TABLE II

Name	No.	Time of Kissing	Result of Animal Inoculation Inoculated October 2, 1916 Killed, December 12, 1916
Patient No. 1 A	K-4	7 A.M.	Tuberculosis.
	K-5	9 A.M.	Tuberculosis.
	K-6	11 A.M.	No tuberculosis.
	K-7	2 P.M.	Tuberculosis.
	K-8	4 P.M.	No tuberculosis.
	K-9	6 P.M.	No tuberculosis.
	K-10	9:30 P.M.	No tuberculosis.
Patient No. 2 B	K-11	7 A.M.	Tuberculosis.
	K-12	9 A.M.	No tuberculosis.
	K-13	2 P.M.	No tuberculosis.
	K-14	4 P.M.	No tuberculosis.
	K-15	6 P.M.	No tuberculosis.

Next a study was made of the bodies of the flies, separating the wings and bodies for inoculation into guinea pigs, all of which developed generalized tuberculosis.

Having demonstrated that the flies kept under these conditions were contaminated throughout with tubercle bacilli, it seemed of interest to determine of how much real practical danger such flies would prove to be to guinea pigs when they crawled over and infected their food.

Five guinea pigs were placed in a box covered with netting and twenty to thirty or more flies were confined with them. As the flies died off they were constantly replaced by others. A receptacle containing sputum with numerous tubercle bacilli in it was placed high in this box. The flies fed on the sputum and on the carrots and the carrots eaten by the guinea

pigs contained fly specks contaminated with tubercle bacilli. The guinea pigs all failed to react to tuberculin given subcutaneously and at autopsy showed no trace of tubercle bacilli.

The details follow:

Fy, 1 *a-b*. The fly specks were washed with sterile saline and inoculated subcutaneously into two guinea pigs. The bodies of the flies were divided in three groups pulverzied and inoculated as follows:

Fy 2, *a-b*. The feet of the flies were inoculated into two pigs.

Fy 3, *a-b*. The bodies of the flies were inoculated into two pigs.

Fy 4, *a-b*. The wings of the flies were inoculated into two pigs.

November 3, 1916, five guinea pigs, Fy 5, 6, 7, 8, 9, were placed in a box covered with mosquito netting. The pigs were fed on carrots. A receptacle containing sputum with tubercle bacilli in it was placed high in this box. Several dozen flies were placed in the enclosure and allowed to feed on the sputum and on the carrots. The pigs, flies, and sputum were allowed to be together in the box for two weeks. It was repeatedly demonstrated that the flies when feeding on the carrots left some specks which upon examination by ordinary staining method contained acid-fast bacilli. It was demonstrated repeatedly that the guinea pigs ate the carrots containing the fly specks contaminated with tubercle bacilli. A dozen fly specks were scraped from the carrots and after being suspended in saline were inoculated subcutaneously in two guinea pigs.

Fy 10 *a*, guinea pig 1 } inoculated November 10,
Fy 10 *b*, guinea pig 11 } 1916.

Summary of Result of the Experiment. Autopsies

December 22, 1916.

Guinea pigs, Fy 1, *a* and *b*, inoculated with fly specks. General tuberculosis.

Fy 2, *a* and *b*, inoculated with feet of fly. General tuberculosis.

Fy 3, *a* and *b*, inoculated with bodies of fly. General tuberculosis.

Fy 4, *a* and *b*, inoculated with wing of fly. General tuberculosis.

Fy 5, 6, 7, 8, 9, which were kept in the box with the flies, sputum and the daily "food" "carrots," appeared to be in perfect health, and December 20, ½ c.c. of 1 per cent of old tuberculin failed to give a positive tuberculin reaction, and at the autopsy all pigs appeared to be perfectly normal and no trace of tuberculosis could be found.

January 3, 1917.

Fy 10, *a* and *b*, killed. Autopsy, moderate tuberculosis.

Discussion and Summary. The results reported here are too few to be used as proof positive in a matter so important as this, but we wished to emphasize one point toward which they incline, namely, that the final gap between the occurrence of tubercle bacilli and proof of infection has not in many instances been adduced. Infected hands do not imply more than the possibility of transference of the tubercle bacilli to another, a fact we have not, so far, established. So, too, with the danger from flies, they become contaminated, and yet the contaminated food is of little apparent danger to guinea pigs.

Tubercle bacilli can easily be transmitted to another by kissing, an act which places them upon the lips, whence they are easily transferred to the mouth, tonsils, and alimentary or respiratory tract.

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MARGINAL SOUNDS

By George E. Bushnell, M.D., Washington, D. C.
Colonel, Medical Corps, U. S. A. (Retired)

SOME years ago the writer called attention to the fact that the sounds resembling râles which may be heard during the inspiration over the costo-pleural space are producible in the normal individual, and that being subject to well-marked and easily discernible laws these sounds must be considered to be concomitant to the normal inspiratory descent of the diaphragm. Further observation has confirmed the correctness of the views expressed in these papers, and the "marginal sounds" have been demonstrated upon the healthy subject to several hundred medical officers of the army during instruction in courses of physical diagnosis. Since these sounds have frequently been mistaken for signs of disease, an understanding of their true nature is of importance in the study of affections of the lungs and pleura.

Select a healthy man, preferably an athlete, who has strong respiratory muscles and knows how to control them, and examine with the stethoscope the characteristics of the inspiration which follows expiration and cough. The breathing is best performed as follows: Starting with a moderate inspiration which passes but slightly beyond the position of rest of the lung, the subject is instructed to expel the air by a forcible expiration which terminates in a short cough and then to inhale immediately, but only sufficiently to return the lung to the former inspiratory position. The respiratory cycle will then consist of a series of moderate inspirations succeeding forcible expirations and the type of breathing will be almost purely diaphragmatic. If the subject has been properly selected and has sufficient intelligence to comprehend and to follow the instructions, the observer, placing his stethoscope over the complemental space in the axilla, preferably the right, will hear during inspiration a number of sounds resembling closely medium-sized moist (sometimes somewhat dry) râles. These sounds are heard but once during an

inspiration over a given portion of the complemental space. They are heard at the beginning of inspiration over the upper part of the complemental space, near the end of inspiration over its lower portion. They follow downward the line of Litten and are heard approximately at the time that this line passes the point of auscultation.

Attach the bell of a stethoscope to each of the rubber tubes of the instrument, closing the free arms of the bells with plugs or with the thumbs. Then placing one bell in an intercostal space in the upper portion of the complemental space and the other bell in the intercostal space immediately below the first, the observer will note that the sounds are heard first with the ear connected with the upper intercostal space and, if the breathing is not too rapid, only after an appreciable interval by the other ear.

When the marginal sounds are well elicited the phenomenon is an interesting one. Numerous rippling sounds are heard—they suggest a wave breaking upon the beach—which plainly enough are produced by a single moving line. The line comes, passes, and disappears; it is heard a moment later by the other ear, still a single line, the sounds entering the stethoscope, passing through it and disappearing in the same way.

If the force of expiration equals that of inspiration, the marginal sounds are producible indefinitely. With the untrained subject, while inspiration is performed with active contractions of the inspiratory muscles, expiration is, as a rule, left to the elastic recoil of the ribs and the abdominal wall. In this case the marginal sounds disappear after a few breaths. But if the subject is instructed to exhale a few times more forcibly than he inhales, the sounds are caused to reappear.

Hitherto it has been assumed that the subject is examined while erect. If he lies upon the side and examination is made for marginal sounds, it will be found that they are produced very distinctly and through a wide range on the lower side, but have disappeared entirely from the upper side or are produced but imperfectly during the most vigorous breathing of the well-trained subject. At the same time percussion will show that the lower lung margin has somewhat descended on the upper side of the thorax and has been pushed up to some extent on the lower side. It will also be apparent that, as has been pointed out by Gerhardt, inflation

of the lung leads to its descent to fill completely the complemental space of the superior side, but that once inflated this lung does not contract readily and freely in ordinary expiration and that in general the respiratory changes of volume of the lower part of the superior lung are minimal in extent. If the subject turns to the opposite side, the phenomena are reversed, marginal sounds appear on the dependent side, they disappear on the formerly inferior, now superior, side, etc. This phenomenon was first described by Morrison under the name of "reversible crepitations" and by him was regarded as evidence of a weak heart.

As Holzknecht and Hofbauer point out, radioscopy of the subject in horizontal lateral recumbency shows that the diaphragm is pushed up on the inferior side and takes an active part and moves through a wide range in moderately vigorous inspiration, while on the superior side the complemental space is obliterated, the diaphragm not being adherent to the chest wall and oscillating like a pendulum during respiration, as if its movement were passive and secondary to that of the inferior half. The explanation given by Holzknecht of the increased activity of the inferior half of the diaphragm is that the abdominal viscera, especially the intestines, being free within certain limits to flow in the abdominal cavity almost like a fluid, fall away in lateral recumbency from the superior side and collect in the dependent side, crowding the diaphragm of that side upward. The diaphragm, which is, of course, dependent upon extraneous help to return to its normally arched position after inspiration, is thus enabled to contract more efficiently and to act through a wider range. Similarly we may say that on the superior side the viscera, tending to fall away to the dependent side, no longer push up the diaphragm, but on the contrary exercise a negative pressure which amounts to traction upon it. Hence the lung readily expands to its full extent in the first full inspiration, but is unable to contract in expiration, since the diaphragm cannot ascend and consequently takes but little part in the later respiratory movements, so long as the force of these movements is not great enough to counteract the traction of the viscera and restore the complemental space upon the superior side.

The marginal sounds heard on the dependent side are then, it would appear, associated with vigorous action of the diaphragm,

but in the upper side where the complemental space is for the time non-existent, they are found to be wanting. There can be no reasonable doubt that they are due to the separation of the diaphragmatic from the costal pleura during the contraction of the diaphragm, which causes the descent of the lung in inspiration. The peeling off of the diaphragm from the chest wall encounters sufficient resistance to cause the depression along the line of separation which we know as the line of Litten. What would be more natural than that the separation of the two moist surfaces against the resistance thus revealed should cause sounds like those now under discussion, produced along a single line, the line at which the separation is taking place at the moment?

If marginal sounds are indeed caused by the separation of the leaves of the pleura, evidently the appellation "marginal" is incorrect. The sounds are really extrapulmonary, though, of course, the margin of the lung is in the closest relation with the place of their production.

It remains to consider the fact that the marginal sounds disappear if inspiration exceeds expiration in force. Evidently this disappearance is to be explained by the relative distention of the lung, which not being a perfectly elastic organ does not return at once to its former condition when the distending force ceases to act. The performance of the lung depends upon its expansibility, not upon its size. In other words, that lung will best expand (and produce marginal râles in so doing) which has been most efficiently emptied in the preceding expiration.

This explains a fact which has led to misapprehension, namely, that marginal sounds are often heard at the base of a tuberculous lung, but are absent on the sound side. Here the tuberculous lung, having lost some of its elasticity on account of the presence of the lesion, does not expand readily during ordinary respiration and the healthy lung does the greater part of the work. But the diseased lung is still capable of expansion, and when the respiration becomes more forcible it expands to a greater extent than does the healthy lung, which has been relatively distended in the previous respirations, and in thus expanding produces marginal sounds.

The importance of marginal sounds is not their interest as a physiological phenomenon, but the fact that they have almost

invariably been considered by the clinician as evidence of a morbid process of some kind. They have been regarded as pleural friction sounds, as râles denoting a basal tuberculous process, as evidence of a basal tuberculous lymphangitis extending from the apex, as relics of former pleurisies or influenzas, as due to mucus aspirated into the lung margin from above, and as a sign of atelectasis. Dry pleurisy at the base is a favorite diagnosis, but the greater part of the clinicians seem to have settled upon atelectasis as the proper explanation, the fact that marginal sounds usually disappear after a few inspirations being interpreted as connected with an expanding atelectasis.

Of course the most unanswerable argument against the supposition that marginal sounds are due to a morbid process of any kind is the fact that they are produced best in the most vigorous subjects, a fact easily verified by anyone who will comply with the conditions governing the production of these sounds.

FATAL HEMOPTYSIS FOLLOWING EXPLORATORY PUNCTURE OF CHEST IN YOUNG CHILDREN

By A. Caillé, M.D., F.A.C.P., New York

At the Thirtieth Annual Meeting of the American Pediatric Society the writer reported two fatalities following exploratory chest puncture as follows:

An infant, six weeks old, was admitted to the hospital with an outside diagnosis of lobar pneumonia. The history chart states that the child weighed 6 pounds at birth and 6 pounds at the time of its admission, the symptoms of respiratory embarrassment dating back two weeks. When admitted the infant was moribund and markedly cyanotic. It had a rapid, jerky, shallow respiration, a rapid, hardly perceptible pulse. Percussion revealed flatness over both lungs posteriorly; pectoral fremitus was absent below the scapula on both sides. To make sure as to the presence or absence of serum or pus, an aspirating needle of moderate caliber was pushed at the seventh interspace, into the dull area of the right thorax for about ¾ of an inch. This procedure was followed by a feeble coughing effort and by a brisk hemorrhage from the mouth and in less than a minute life was extinct.

At the autopsy the foramen ovale was found patent, presenting a slit-like opening 2 mm. in diameter. Beneath the leaflet of the mitral valve there was an opening in the interventricular septum about 8 mm. in diameter. The cardiac musculature was of about the same thickness on the right as on the left side. There was a distinct inflammatory consolidation in both lungs and marked congestion of the entire lung.

There was an extensive hemorrhage into the right pleural cavity, and there may have been fluid in this cavity, but it was obscured by the hemorrhage. The track of the needle in the lower quadrant of the middle lobe could be followed for ¼ of an inch and a puncture of a larger blood vessel could not be made out. There was no laceration of the lung tissue.

Histological Examination (by Dr. G. L. Rhodenburg). Histological examination of the lung, in the area marked as having been the site of puncture, shows the alveoli to be more or less completely filled with blood cells and fibrin. A demonstrable lesion of any of the larger blood vessels is not in evidence. The walls of the capillaries throughout the area,

however, are in many places ruptured, and hemorrhage has evidently occurred through these breaks. The ruptures are apparently not mechanical in origin, for the capillary wall is dissolved rather than torn. Whatever this lytic agent has been, it has acted focally, since there are considerable areas in which the capillary walls are intact.

Another fatal sequence to an exploratory puncture came under the writer's observation about fifteen years ago. A feeble, poorly nourished cyanotic child two years old was admitted to the hospital service of a colleague after a two weeks' illness, with a high temperature, signs and symptoms of a right-sided pulmonic consolidation, and urgent respiratory embarrassment. Vocal fremitus was not in evidence and respiratory sounds were indistinct. To make sure as to the presence or absence of serum or pus, a needle was introduced. Fluid was not aspirated, and on withdrawing the needle a brisk hemorrhage from the mouth took place and the child was dead in a few minutes. An autopsy was not granted.

Comment. Fatalities from exploratory puncture of the thorax are exceedingly rare. In the annals of the American Pediatric Society, now extending over a period of thirty years, no such occurrences have been reported. In my own clinical experience of forty years, during which many thousand exploratory punctures have been performed, the two cases here reported stand out prominently. I can recall, however, several instances in which a puncture in adults was followed by streaks of blood in the sputum, with a prompt return to the normal after a day or so. To plunge a needle *lege artis* into the lower thorax is considered a harmless procedure by the diagnostician. The indications for exploratory puncture are definite and frequently imperative as a life-saving inquiry. On the other hand, the precise conditions under which a simple puncture may be hazardous should be carefully considered.

The capillaries of the lung vary greatly in capacity, and they can take up a very large quantity of blood when cardiac insufficiency or pulmonary inflammation induce pulmonary congestion. Recent experiments by Kuno of the Japanese Medical School at Mukden have shown that the amount of blood which the lungs can hold varies from 9 to 19 per cent of the total amount of the blood of the body. Thus if a highly engorged lung be punctured, a localized hematoma may result, and if, in addition, the clotting time of the blood is altered and prolonged, as in hemophilia and in cachectic

individuals with an acquired lytic or hemorrhage diathesis, a free hemorrhage into the pleural cavity and trachea may take place.

In the first case cited a chronic congestive condition of the respiratory tract existed from birth, due to the pronounced congenital heart defects.

In the second case an extreme congestion of the lung was brought about by the pneumonic infection and inflammation, accentuated by cardiac insufficiency as a result of two weeks' strain upon the heart of a feeble individual. In neither case was the hemorrhage due to a faulty technic.

The practical lesson to be drawn for the guidance of the clinician is to bear in mind that in acute cases in which a puncture seems indicated, the introduction of an exploratory needle into the thorax containing a highly congested lung is attended with some degree of risk when cyanosis and other characteristic signs point to cardiac or circulatory failure. In obscure, subacute, and chronic conditions an *x*-ray investigation should precede and may obviate the necessity of a puncture. When exploratory puncture of the chest is performed for the purpose of eliciting the character of an exudate or transudate, which otherwise reveals its presence by characteristic physical signs, including a bulging of an intercostal space during inspiration, the danger of an internal hemorrhage is practically *nil*. Extreme collapse and sudden death without visible hemorrhage, following exploratory puncture of the chest, has also been observed and must be attributed to shock when an autopsy reveals absolutely nothing to account for the fatal outcome.

A CLINICAL STUDY OF THE COMMUNICABLE DISEASES

OBSERVED AT UNITED STATES ARMY GENERAL HOSPITAL NO. 6, FORT McPHERSON, GA., FROM OCTOBER, 1917, TO JANUARY, 1919

By C. N. B. Camac, Lt.-Col. M.C., U. S. A.

IN the brief period from the establishment of the first military encampments of the United States Army in this country in 1917 to the beginning of demobilization in 1918 medical science has had an unprecedented opportunity to study communicable diseases. This opportunity has made possible the application of preventive measures, tested and proven to be effective, thus eliminating heretofore destructive diseases, for example, typhoid fever. It has also been possible, by treatment and in some cases by preventive measures, to hold in check such diseases as diphtheria, lobar pneumonia, and meningitis. On the other hand, certain diseases, for which no preventive or treatment is known, have appeared with alarming severity and in epidemic or pandemic form. Chief among these are measles and influenza. Because of the great number of those stricken, exceeding any figures known to practitioners and laboratory workers, features of these diseases have revealed themselves which have necessitated an entire change of thought with regard to their etiology, prevention, curative treatment, and relative severity. For example, measles, at the beginning of 1917, was not looked upon as one of the dangerous infections. Again, much doubt existed regarding the severity of influenza. Measles crept in insidiously, influenza burst more as a storm. When the deaths in these two epidemics occurred in increasing numbers, the clinicians and pathologists in all the encampments, aided in every way by the Surgeon General's Office, immediately began an intensive study, with the result that methods of prevention and treatment were promptly tested, and in consequence a new chapter in communicable diseases has been written.

This paper records some of the observations made and lessons learned at United States Army General Hospital No. 6, Fort McPherson, Ga., an institution of from 1800 to 2100 patients. To this number may be added the personnel of the hospital, consisting of some 75 officers, 142 nurses and aids, and 961 Hospital Corps men, on all of whom protective vaccination was practiced, and 150 Quartermaster Corps. The neighboring War Prison Barracks, Hospital Unit Training encampments, and Reclamation Camp (Jesup) also offered material for preventive vaccination, and sent to General Hospital No. 6 cases stricken with the various diseases. The patients were received principally from Camp Gordon, about fifteen miles away, but also from various encampments in the South where Base Hospitals had become crowded by the rapid development of the epidemics. A population of some 6000 persons were, therefore, living under somewhat similar conditions.

The diseases brought in epidemic form to the hospital at this Post were: Mumps, measles, lobar pneumonia, and influenza.

Other communicable diseases not in epidemic form were: Meningitis, diphtheria, typhoid and paratyphoid, smallpox and scarlet fever.

Mumps. There were about 600 cases of this disease. Besides the common complication of orchitis, which in a few cases was double, the two rarer complications of pancreatitis and meningitis occurred. Pancreatitis attacked 7 or 8 cases, and was manifested by severe pain and great tenderness in the upper abdomen, together with marked prostration. The patients were attacked suddenly, rapidly assuming the appearance of being seriously ill. There was slight nausea, but no vomiting. The abdomen was not rigid. With this exception the facies, prostration, and abdominal tenderness suggested acute peritonitis. The temperature was not significant. The severity of the attack lasted about twenty-four hours and no serious features developed. There were 3 cases which showed mild meningeal symptoms, but this, too, was of short duration, and lumbar puncture was not indicated. Two cases developed incomplete hemiplegia which persisted for several weeks and gradually disappeared. There was no mortality in this epidemic.

Measles. Of this disease 500 cases were observed. Caps, gowns, masks, and the sheet cubicle system were employed, with the result

that only a very small number of nurses and Medical Corps and no physicians were attacked. The cases were composed entirely of soldiers from neighboring encampments. The pulmonary complication was the only feature of importance, and this, as has been amply shown throughout the military hospitals, was among the gravest pathological conditions with which the military physician had to deal. At the time this epidemic appeared our bacteriological studies could not be pursued very intensively on account of our being dependent upon the Department Laboratory, four miles from the hospital; the hospital laboratory was not equipped to make more than routine bacteriological examinations. We were, however, able to make sputum, naso-pharyngeal, pleural, and post-mortem cultural studies in many of the cases, and *Streptococcus hæmolyticus* was the prevailing organism. The clinical features were significant. The typical course was of a measles for six or seven days with a fall in temperature coming to normal and remaining so for two or three days. The patient would then suddenly develop an acute pharyngitis, marked aphonia, epistaxis, and a sudden rise of temperature to 103° and 104° F.

Auscultation of the lungs revealed large, moist, bronchial râles. There were no physical signs of lobar consolidation, nor did post-mortem findings reveal such. From the first, the patients complained bitterly of pleuritic pain, very acute in character, usually on one side. In the cases which pursued a serious or fatal course, very fine crepitant râles became evident about the second day following the rise in temperature, with an effusion into one or both pleural cavities, at first serous or sero-sanguineous in character, having a tendency to become purulent very early. At the beginning there was profuse expectoration, yellow and glairy in appearance, without the tenacity of that of lobar pneumonia. It was markedly streaked with bright blood, not blood-stained. In those cases becoming critically ill the expectoration became scanty and frothy in character on about the third or fourth day. The pleuritic pain was not relieved by the pleural effusion.

Cyanosis, a very early manifestation, appeared as soon as the second day after the sudden rise of temperature. It manifested itself first on the lips, then on the extremities, nails, face, and skin about the neck.

The principal symptoms complained of by the patient were—first, a sore throat, congestion of the nasal mucous membrane, with profuse epistaxis; then a feeling of tightness across the chest, and dyspnea, with very acute pleuritic pains. The patients would allow themselves to be moved in bed only under protest. Brown crusts covered their lips, which became deeply indented. This in spite of careful nursing. Harassing, irritating cough persisted.

The blood pressure in these cases averaged 90 to 95 systolic, and 60 to 75 diastolic. The pulse and respiration ratio averaged three to one.

The cases running a fatal course generally died within the first week, sometimes in three or four days. Those surviving passed through protracted and tedious convalescence. Functional aphonia persisted and for weeks after all other symptoms and signs had disappeared. *X*-ray plates of those who recovered showed no pathological shadows beyond those of pleural thickening and adhesions. In only a few instances was the pneumococcus demonstrated in the sputum, the *Streptococcus hæmolyticus* predominating. Cultures from the pleural effusions also demonstrated the *Streptococcus hæmolyticus*.

Cyanosis was the most serious manifestation, for soon after its appearance the cases would seem to gradually drown in the outpouring exudate. This could be detected in its rapid increase first by fine crepitations over the entire chest, which within a few hours would increase to larger and more distinctly audible râles, until the gross gurgling could be heard without a stethoscope, and finally bubble up from the trachea and overflow from the mouth with no effort of coughing. The exudate at this stage was usually a faint pink color and sometimes distinctly red and frothy. So completely had the initial attack of measles disappeared in some cases that they were up and about the wards and others were ready for discharge when this secondary infection attacked them, and in many cases would prove fatal.

At post-mortem examination the lungs showed intense engorgement and congestion upon sectioning, presenting a very dark red appearance, in some instances almost black. Air could be expressed from the alveoli and tubules, but not much accumulated secretion; nor were there any signs of pulmonary consolidation. Portions of pulmonary tissue, immersed

in water, would float. Upon sectioning the bronchial tube, the endothelium was of a dark brick color, intensely engorged, granular in appearance and blood-stained. This generally was the appearance of the entire lung, though in a few cases a lobe or so partially escaped. Effusion was found in one or both pleural cavities, pleuritic adhesion obtaining on the dry side, while the side containing the fluid exhibited much plastic exudation—the fluid being sero-purulent, or sero-sanguineous. Pleural effusions were demonstrated by the aspirating needle in 35 per cent of all this class of cases. The bacteriological findings have shown the *Streptococcus hæmolyticus* to be the infecting agent in this secondary infection following measles.

Fourteen cases developed empyema. Of these 11 were treated by rib resection and drainage, all of whom eventually succumbed. The remaining 3 were treated by thoracentesis, a large trochar being used and the cavity irrigated with Dakin solution. This whole subject of empyema treatment has been so fully discussed by the Empyema Commission that our figures merely are recorded here. Climatic conditions should be taken into consideration in judging the reports from various camps. The report from Camp Zachary Taylor in Kentucky points out a wave-like character in the severity of the attacks. In our cases those which developed late in the winter were more prone to the serious pulmonary complication.

The percentage of deaths in 500 cases was 2.4. The mortality among those with pulmonary complication was 27 per cent.

Conclusions. 1. Measles as seen in the young robust individual is a harmless exanthem.

2. A secondary grave manifestation, often not appearing till convalescence, the patient being up and about, is a *Streptococcus hæmolyticus* infection.

3. While this complication is systemic in its effects, the respiratory passage and pleuræ are the chief points of attack.

4. The pulmonary complication is an intense inflammation of the entire respiratory lining (pneumonitis), with a flooding exudate in which the patient drowns, the process being too rapid for the development of a lobar consolidation, which is extremely rare, or for typical broncho-pneumonia, which is also rarely found. Pleural exudates (serous, sero-sanguineous and purulent), sometimes appearing in both pleuræ, are common. The pericardial and peritoneal cavities are sometimes attacked.

5. Unlike lobar pneumonia, measles renders the victim very susceptible to cold. Out-door treatment, as practiced in lobar pneu-

monia, should not be employed. Fresh, warm air should be supplied and great caution to avoid exposure, during convalescence especially, should be exercised.

6. Pleural exudates. See report of Empyema Commission.

7. Protective vaccination offers the greatest promise of combating this complication.

Lobar Pneumonia. Of this disease 139 cases came under observation, to which may be added 300 cases, convalescent, from Camp Wheeler.

I. Pneumococcus Alone

Type Uncomplicated	Incidence	Recoveries	Deaths	Mortality, Per Cent
Type 1	26	25	1*	3·8
Type 2	18	17	1*	5·5
Type 3	10	10	0	0·0
Type 4	27	27	0	0·0
Total	81	79	2	2·4

* Note: acute nephritis—Autopsy.

II. Pneumococcus and Streptococcus

Type 1	3	2	1	33·0
Type 2	0	0	0	0·0
Type 3	0	0	0	0·0
Type 4	2	1	1	50·0
Total	5	3	2	40·0

III. Streptococcus Alone
(Hemolytious or Viridans)

	11	5	6	54·0

IV. Undetermined
(Not Pneumococcus or Streptococcus)

	39	38	1	2·2

V. Miscellaneous

Pneumo Type 1 and 2	1	1	0	0·0
B. Influenza	1	1	0	0·0
Staphylococcus in throat	1	1	0	0·0
Total	139	128	11	7·9

Method of Procedure. Immediately upon the finding of clinical signs indicating an area of consolidation the patient was desensitized with polyvalent antipneumococcus serum (Mulford's) and placed in a pneumonia ward.

Clinical Features. The three striking features have been: (1) Variations in temperature, (2) the rapid recovery, (3) absence of profound toxic effects. The rapid breathing, flushed face, and further manifestations of profound toxemia were absent in the majority of our cases (treated with serum) unless complicated by some other septic organism. A careful inspection of our temperature charts fails to reveal any uniformity of the lobar pneumonia curve. Invasion by another organism is usually accompanied by a greater variation in the curve, but a number of the cases in which no other organism could be demonstrated have shown a temperature decline with a step like lysis similar to that of typhoid, but without the long typhoid period of decline. Extension of the pneumonic process or involvement of another lobe is marked by a sharper and more sustained rise, whereas invasion by another pyogenic organism presents a more gradual rise and shows greater variations. About 5 per cent of the cases show the sustained temperature with the sharp critical fall commonly described as characteristic of the pneumonia curve. The leucocyte count, beyond indicating a good prognosis when high, has been no guide as to the development of complication or extension of the process.

Complications. Empyema and otitis media were the most frequent. The former of these has been dealt with in a separate report. (Report of Empyema Commission.) Two cases presented pneumococcus abscesses of the abdominal wall. Streptococcus pericarditis occurred in 2 cases, mediastinal abscess in 1 case. Meningitis in 1 case only. Acute nephritis occurred in about 15 per cent (as evidenced by albumin and casts) in uncomplicated cases, 75 per cent in complicated cases.

Serum Treatment. The amount of serum administered has varied between 50 c.c. and 600 c.c., with an average of 250 c.c. About 10 per cent of the cases did not require serum treatment. In the military service it is possible to begin the serum treatment much earlier than in civil practice. Few of our cases came under treatment later than the third or fourth day, and many of them were treated in the first forty-eight hours. Treatment was begun on the detection of the first clinical sign, without waiting for differentiation of type. For this purpose polyvalent serum was used. (1) If the case showed Type I this serum was used, otherwise polyvalent serum

was continued. No systematic blood cultures were made on our cases.

Serum Sickness. About 50 per cent of the cases showed signs of serum reaction. These ranged from simple erythema to the extensive urticaria, with general swelling and joint pains. Some of the severer cases developed after 50 c.c. of serum had been given and others showed no reaction after 400 to 600 c.c. Manifestations appeared from twelve hours to fourteen days after administration. Only 2 cases showed any alarming features. One of these had blood and blood casts and excessive amount of albumin in the urine. The other, who received only 50 c.c. of serum, with prompt fall of temperature which remained normal, two weeks later developed general swelling, making him unrecognizable, together with swelling and pains of many of the large and small joints and with albumin and hyaline casts in the urine, all of which disappeared in five or six days.

Anaphylaxis. Only 1 case presented symptoms of anaphylaxis. This was a case of asthma of unknown cause. In desensitizing him he showed no reaction, but when 80 c.c. of serum had been administered, cyanosis, dyspnea, with asthmatic breathing, cold sweat, disturbed, rapid heart action and general signs of collapse developed. Administration of serum was continued up to 100 c.c. and subcutaneous injection of adrenalin was given. In twelve hours the temperature was normal and continued so, requiring no further treatment.

Streptococcus Infection Alone and Complicating Pneumococcus. Reference to the table shows the frequency of this condition. At this time we had not practiced streptococcus vaccination. (See "Influenza," p. 384.) With the accumulation of evidence it is becoming more and more apparent that when this organism is added to pneumococcus infection the case assumes grave features. The destructive power of the streptococcus is well demonstrated in the pulmonary complication of measles, in which the pneumococcus is rarely found. In reviewing the records one is disposed to conclude that it is the streptococcus, superimposed upon pneumococcus, that gives lobar pneumococcus pneumonia its real virulence. Early treatment with serum seems to lessen the tendency toward the development of this mixed infection. While slight yellow tingeing

of the conjunctiva is common in this disease, we found marked jaundice of the conjunctiva more common in those cases of streptococcus infection alone, and in penumococcus pneumonia complicated by streptococcus.

Important Points. (1) Early diagnosis is essential. (2) Clinical signs of consolidation should be followed by immediate use of polyvalent or other serum. (3) If more than 250 c.c. of serum are required and the temperature and toxic signs continue, complication by other organism should be suspected; like malaria when treated with quinine, the pneumococcus infection is rapidly overcome by serum. (4) Uncomplicated pneumococcus infection is a comparatively harmless and rarely a fatal condition. (5) Colored men are more susceptible, possibly because they keep up and about longer and come under treatment late. Their complaints are apt to be disregarded by line officers, who think them shirking. (6) Leucocytes are not a reliable guide in determining the added streptococcus infection. Mononuclear increase is not a guide in determining serum temperature rise from septic temperature. (7) Protective streptococcus vaccination should be employed. (8) Diet, 2000 calories; 3000 c.c. of water should be administered daily (2).

Influenza. Towards the latter part of September, 1918, this epidemic appeared in the Southern camps. Unlike the measles, which took many weeks to reach the height of the infection, this epidemic rapidly assumed severe features and proportions. In the North it had been in progress for some weeks before appearing in the Southern camps, and before that the troops and civilians of many nations had been attacked, constituting a true pandemic. Profiting by this warning, the Laboratory of U. S. A. General Hospital No. 6, which was by now fully equipped, instituted immediate bacteriological studies upon cases admitted to the hospital. Sputum and naso-pharyngeal bacteriological examinations were carried out by Capt. Moffit, Chief of the Pathological Laboratory, with the result that *Streptococcus hæmolyticus* was found in an overwhelming majority of the cases. A vaccine was prepared, and through the prompt co-operation of the Commanding Officer, Colonel T. S. Bratton, universal inoculation by Special Order was practiced upon everyone on the Post and in neighboring encampments. In addition the lipoid antipneumococcus vaccine was given.

Thus with few exceptions the entire personnel of this community was immunized. The full bacteriological report will appear elsewhere. Clinically our observation was that the immunized cases which came down with the infection were few in number and were not as ill as the unimmunized, and that no deaths occurred among those who had been so immunized. Exceptions to these statements were among those who had been stricken after one inoculation. There were over 600 cases under observation. Only 7 of these showed the Pfeiffer bacillus in the sputum, 13 in the nasopharynx. There were 17 deaths.

General Management of the Epidemic. We used six wards, averaging fifty beds each, for influenza cases. It was possible in each of these wards to make the following subdivisions of cases: (*a*) Observation, (*b*) fully diagnosed cases, (*c*) pneumonia complications, (*d*) convalescents.

Mouth and nose masks were worn by doctors, nurses, and corps men, and also by patients when convalescent. These masks were made at first of two-ply and later of three-ply gauze. The sheet-cubicle system was employed. Thermometers were wholly immersed in flat dishes of cresol or bichloride solution. Basins of cresol solution were placed about the wards for the use of attendants. Dichloramine T or chlorocozane spray, 2 per cent, was used on the nasopharynx of patients and attendants. Protective inoculation of antistreptococcic vaccine was employed, early in the epidemic, on all those not yet affected. A total of 3 c.c. of the antistreptococcic vaccine was administered, divided into three, four, or five doses. Lipo-pneumococcic vaccine was administered at the same time. The entire command was treated in this manner with a few exceptions, some refusing, others being taken down with the disease before inoculation. For ordinary cases the only drug used in addition to the nasopharyngeal spray was aspirin and the ordinary laxatives.

Pneumonia cases were immediately isolated and, if lobar, were treated with Mulford's antipneumococcic polyvalent serum without waiting for type determination. This, however, was determined as soon as possible by the laboratory, and those cases which were Type "1" pneumonia were treated with Type "1" serum,—otherwise the polyvalent serum was continued. The cultures from nasopharynx and sputum, as well as the autopsy findings were *Strep-*

tococcus hæmolyticus, with occasionally a catarrhalis or staphylococcus in throat cultures, except in a few cases. In 13 cases the nasopharyngeal cultures showed the Pfeiffer bacillus and in 7 cases the sputum showed this organism. Cases seen early who were kept in bed, and who were placed immediately under treatment with antipneumococcic serum if lobar pneumonia appeared, uniformly did well. The mortality was principally among cases brought in from Camp Infirmaries after the soldiers had been ill five, six, or seven days. These cases were usually rapidly fatal. Soldiers without complications were returned to duty after ten days of normal temperature.

All deaths were from pneumonia complications except 1 case, a nurse, which was a streptococcic septicemia with probably a terminal pneumonia. This case was rapidly fatal, having general purpura and showing the other clinical features of sepsis. The blood culture in this case was not taken and no autopsy was done. To December 20, 1918, 495 cases of this disease came under treatment with 16 deaths —a mortality rate of 3.2 per cent. This low death rate is not due to the fact that we got a more thoroughly seasoned lot of men, and therefore more resistant to the disease. We drew our cases from camps where the new draft men were being given their preliminary training, from casuals en route, from our own detachment, as well as from the seasoned troops at home and overseas.

The climate at Fort McPherson is ideal for the treatment of these acute conditions, and a large measure of our success may be attributed to this natural advantage. Another factor which we feel aided greatly in the care of these cases was that a graphic chart of the temperature, pulse, and respiration was kept on the wall at the head of the bed, and the nurse recorded each reading *at the time it was taken*. In this way the officer in charge had a picture of the condition of his patient always before him. The laboratory too was in close daily co-operation with the clinician. The diagnosis was made microscopically as well as clinically and the bacteriology of the case was watched until convalescence.

Clinical Features. Those who had seen the measles epidemic remarked on the striking similarity in the pulmonary complication in these two diseases. When the bacteriological reports accumulated this similarity was explained. We are aware that other military

laboratories have not found this preponderance of *Streptococcus hæmolyticus*. Captain Moffit, Chief of the laboratory, was in communication with these other laboratories, and every method recommended for detecting the Pfeiffer bacillus was employed, and still the *Streptococcus hæmolyticus* was the prevailing organism. When, therefore, we record the clinical features we may refer to those listed under the pulmonary complication of measles. There were the following exceptions: the influenza cases were not so rapidly fatal, and the cyanosis and intense inflammations of the respiratory passages were not so marked. Lack of space forbids a more detailed account of the cases here, but we believed that the most important fact to emphasize is that in each epidemic the streptococcus was the serious infecting organism. The height of the epidemic was in November, extending from September through December. A second wave of less proportion and severity occurred the latter part of December and in January, but the organism preponderating was Type IV pneumococcus.

Summary. 1. *Streptococcus hæmolyticus* is the prevailing organism.

2. The great similarity between the effects of this organism in the pulmonary complication of measles, and in the similar complication of so-called influenza. Each complication is primarily due to streptococcus.

3. The importance of early inoculation. (Streptococcus and pneumococcus.)

4. The Pfeiffer bacillus alone and the pneumococcus alone (the latter when treated with serum early) are comparatively harmless infections.

Communicable Diseases which did not Appear in Epidemic Form: *Meningitis, Diphtheria, and Paratyphoid, Smallpox, Scarlet Fever*. It is noteworthy that, though these diseases occurred, methods of preventive inoculation confined them to the sporadic stage. Meningitis in some camps assumed epidemic proportions. At U. S. A. General Hospital No. 6, there were 15 cases of the disease with 2 deaths. (3) The most distressing feature in some of the cases was the weakness and pain in the lower extremities, lasting many weeks after subsidence of the acute stage. This disease, together with diphtheria, presented difficulties from a military viewpoint with regard to carriers. By careful observation and isolation of such

cases both in the hospital and training camps we believe that twice at least outbreaks were averted.

Typhoid and paratyphoid appeared in 5 cases only, notwithstanding a contaminated water supply and an outbreak of these infections in the neighboring town of Atlanta. There were no deaths in this hospital. The cases in which the disease appeared had not been inoculated or had not completed full treatment with saline vaccines.

Scarlet fever appeared in 5 cases only, with no deaths.

Conclusion. We observe two groups of communicable diseases.[1] First mumps, measles, pneumonia, and influenza. All four developed to epidemic degree and the latter three claimed many deaths. In all four of these no protective treatment is known. Second a group (meningitis, diphtheria, typhoid, paratyphoid, smallpox, scarlet fever) in three of which protective inoculation has been proven to be effective and in two of which abortive treatment is available. With these formerly destructive diseases no epidemic occurred. Death occurred among the meningitis cases only, and for this disease no preventive inoculation is as yet known.

INCIDENCE AND MORTALITY SUMMARY

Diseases	Incidence	Pulmonary Complications	Deaths
Mumps	600	—	0
Measles*	500 Winter 1917 to 1918	43	12
Pneumonia, lobar	139 Oct., 1917 to May, 1918	—	11
Influenza†	495 Sept. 15 to Dec. 20, 1918	53	16
Meningitis	15	—	2
Diphtheria	6	—	0
Typhoid and paratyphoid	5	—	0
Smallpox	4	—	0
Scarlet fever	5	—	0
Total	1769	96	41

* There were additional cases admitted towards the decline of the epidemic, but there were no deaths among these.

† About 100 additional cases were admitted after this date with one death. These additional cases represent the second wave and showed for the most part pneumococcus Type IV.

[1] The *disease* which claimed the greatest number of deaths is *Streptococcosis*, and for this intensive study is demanded.

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2. For other treatment, diet, heart stimulants, open air and abdominal distention, see *Am. J. M. Sc.*, CLVI, No. 6.
3. For full report see *Arch. Int. Med.*, January, 1919, XXIII, 17-32.

DEFECTS IN MEMBRANOUS BONES, EXOPHTHALMOS, AND DIABETES INSIPIDUS

AN UNUSUAL SYNDROME OF DYSPITUITARISM; A CLINICAL STUDY

By Henry A. Christian, M.D., Boston, Mass.

(From the Medical Clinic of the Peter Bent Brigham Hospital, Boston, Mass.)

THE case whose report follows appears to be almost unique, and is reported primarily for the rarity of occurrence of the extraordinary defects in the skull bones which, with the associated exophthalmos and diabetes insipidus, make a truly remarkable clinical picture. The diabetes insipidus and its reaction to pituitary substance make certain a causal relation between a derangement of the function of the pituitary gland and the increased urinary output. The fact that the only two additional cases with similar skull defects I have been able to find reported in the literature had evidence of disturbed pituitary function makes it probable that the bone changes, too, owe their origin to dyspituitarism. Hence in reporting this case we are calling attention to an effect of pituitary change not generally recognized. Finally this case has given the opportunity to make observations on the effects of pituitary substance given in various ways.

The patient, A. S., Med. No. 7945, a little girl aged five years, was admitted to the Peter Bent Brigham Hospital on January 24, 1918, referred by Dr. Thomas E. Lilly of Shirley, Mass. She remained under observation in the hospital for six months. Her history is as follows:

Family History. Father, mother, and brother 3½ years old are living and well. The boy is normal in every way according to the father's statement. The mother has had no miscarriages.

Past History. The patient was born in Shirley, Mass., of Austrian parents and has lived in Massachusetts all her life. She is the first child and was born at full term after forceps delivery. Her birth weight is not known, but she was of medium size and was breast fed for one year. During this time she grew normally, getting her teeth at the normal time, and had no symptoms of rickets. She had mumps three to four months ago. There have been no other acute illnesses. Past history otherwise is negative.

Weight. For the past year she has weighed about 43 pounds, her greatest weight.

Present Illness. According to the father's statement, the patient was well and normal in every way until three years old. At that time her teeth began to decay and become loose and her gums became swollen and tender. No other symptoms were noted. Her mouth continued to be sore, and at the age of 3½ years the right eye became prominent and she began to drink more water and pass her urine more frequently. These symptoms gradually increased in intensity until both eyes were markedly protruding and she was drinking 9 quarts of water a day and urinating every hour. She has complained of more or less constant pain in her head for two years. Her hearing has gradually become poorer. Her father thinks she has had no disturbance of vision and she has had no vomiting. For four or five months she complained of a little pain in her back and three months ago had a little dysuria for a short time. At times her feet and hands become hot and sweaty. (History obtained through father, who speaks little English.)

Physical Examination. The patient is poorly developed and nourished, lying quietly in bed and apparently fully conscious. Skull symmetrical. Over the whole skull but most marked over the posterior portion are numerous small, smooth irregularities. Both fontanelles are closed. In the right fronto-parietal region and in the left parieto-temporal region are two irregular areas of softening each measuring 8 cm. in its greatest extent. Two similar smaller areas are also present in the left frontal region and on the forehead just above the nose. Both pulsate with each heart beat and bulge when the patient cries, otherwise there is no bulging. The circumference of the head in its greatest diameter is 50 cm. There are no areas of tenderness.

Eyes. Pupils are equal, regular and react to light and accommodation. The scleræ are blue. There is a slight lacrymation. No photophobia, diplopia, nystagmus, or palsies. There is an extremely marked degree of exophthalmos (Figs. 1 and 2) with lid lag (Von Graefe's sign). The eyes can be held in convergence (no Moebius' sign). The conjunctivæ are rather pale. The eyes are definitely tender. No gross disturbance of vision. No glasses worn. No edema of lids. Both lids are somewhat reddened, are thin, and the vessels stand out prominently. This condition is slightly more marked on the right. Ophthalmoscopic examination is not satisfactory. The inner margins of the disks are blurred, the outer margins distinct and raised. The veins are tortuous and prominent.

Ears. Patient hears if one talks in a loud tone. A watch held against either ear is apparently not heard. (Child is very diffident, so this test

of hearing is probably not accurate, and later on there was no evidence of deafness.—H. A. C.) No stigmata, tophi, or discharge. Mastoid processes not enlarged; no mastoid tenderness.

Nose. Both inferior turbinates are thickened, and the patient breathes through her mouth all the time. No discharge.

Mouth. Breath is slightly foul. No ulcerations, exudate or pigment. Lips are of good color and without herpes, ulcerations, or fissures. Teeth.

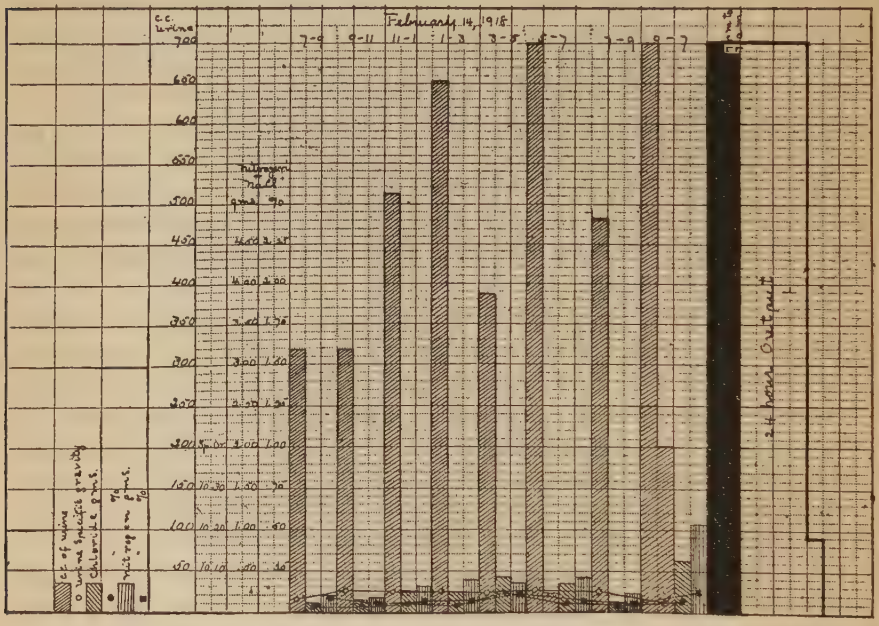

CHART I. "Two-Hour" Renal Test, Showing Fixation of Specific Gravity and Percentage Concentration of Sodium Chloride and Nitrogen during Period of Polyuria. Columns Indicate Amounts of Urine in c.c. and of Sodium Chloride and Nitrogen in Grams; Each Series of Three Corresponding to a Period of Urine Collection. The Circle Indicates Specific Gravity; the Dot Percentage Concentration of Sodium Chloride and the Square Percentage Concentration of Nitrogen. Black Columns at the Right Indicate the Night Amount of Urine; Uninked Columns Indicate Day Amount of Urine.

The second set of central incisors are through. Several of the other teeth are loose and some are missing. There are a few cavities. All are ill-kept. Gums retracted around part of the teeth and are ulcerated as though about to bleed. Pus can be expressed from along several of them and the gums in places are coated with a thick dirty-brown exudate. No leadline. Tongue is heavily coated with a light-brown coat. The papillæ show up prominently. The tongue is protruded in the median line without tremor. No mucous patches or scars. Tonsils are not seen. Pharynx is covered with

FIG. 1. FRONT VIEW OF HEAD.

Showing the Exophthalmos, Causing a Wide Aperture between the Eyelids. (See p. 391.)

FIG. 2. LATERAL VIEW OF HEAD.

Showing Prominence of Eyeball. (See p. 391.)

the same dirty-brown exudate that is on the tongue and gums. Palate and reflexes normal. Larynx. Voice is of good quality.

Neck. No enlargement of thyroid. No palpable lymph glands. Small pulsations are visible in the cervical vessels. The patient holds her head slightly bent forward and objects to having it lifted or turned sideways. No tracheal tug.

Examination of thoracic and abdominal viscera is entirely negative.

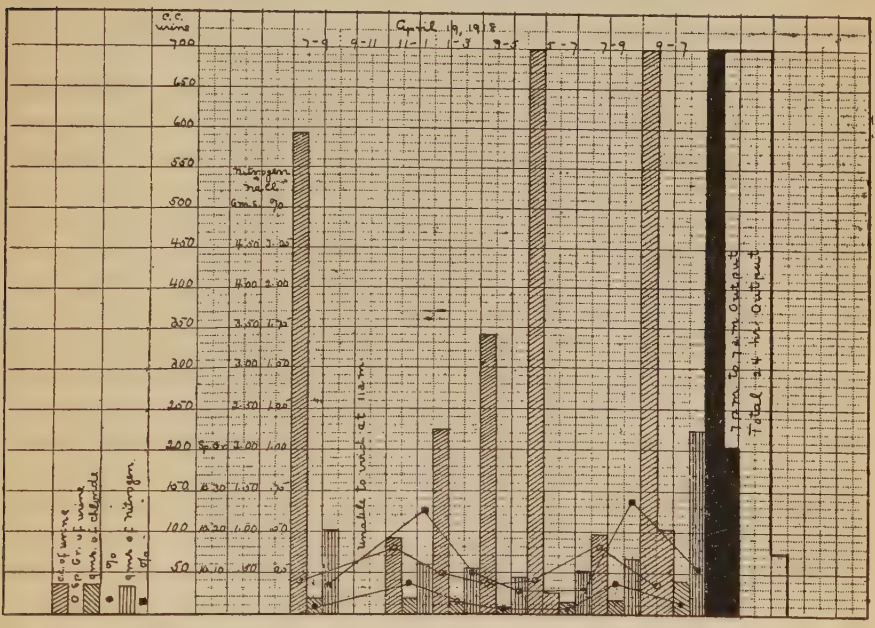

CHART II. "Two-Hour" Renal Test, Showing Absence of Fixation of Specific Gravity and Percentage Concentration of Sodium Chloride and Nitrogen during Period of Normal Urinary Output, While under Influence of Pituitary Substance Given Subcutaneously. For Explanation of Chart see Legend under Chart I.

The Wassermann reaction on the blood serum was negative. Study of the stools was negative. Blood examination showed a red blood cell count of 5,200,000 and a white cell count that ranged between 6600 and 12,600, with an occasional rise to 14,100, 15,600, and 20,100. The differential count on admission showed polymorphonuclear cells 30 per cent, lymphocytes 45 per cent, large mononuclears 23 per cent, and eosinophiles 2 per cent. The urine was normal except for the low specific gravity during the periods when there was a polyuria. The specific gravity then ranged from 1001 to 1004. Under the influence of pituitary substance, when the amount decreased the specific gravity of the twenty-four-hour specimen rose to

1008 or 1010. On February 14th, during the period of polyuria with an output of 5250 c.c., a two-hour renal test was made, as shown by the accompanying chart (Chart I). On April 19th, with a decreased output under the influence of pituitary substance, the output of urine amounting to 2900 c.c., a two-hour test (Chart II) in contrast to the first one shows a very considerable ability to concentrate, as represented by a specific gravity varying from 1007 to 1016, a percentage concentration of sodium chloride varying between .02 per cent and .19 per cent, and a percentage concentration of nitrogen varying between .13 per cent and .69 per cent, as shown in the chart; in other words, a normal picture.

The excretion of urine in relation to dosage with pituitary substance was of much interest. Chart III shows this graphically. The solid dot represents the urine output for each twenty-four hours; the circle the fluid intake. The arrows show the time of beginning and ending dosage with pituitary substance. The letters in reference to the key show the form of pituitary substance, dosage, and mode of giving. It is evident in the chart that at *A*, *E*, *F*, and *I* there is a definite decrease in urine output and fluid intake. At these periods the patient received pituitrin (Parke, Davis & Co.), a liquid extract of pituitary gland, given subcutaneously in varying dosage. In contrast gland substance taken by mouth and swallowed, *J*; gland substance mixed in gum drops and allowed to dissolve slowly in the mouth for local absorption, *B* and *C*; and gland extract (pituitrin, Parke, Davis & Co.) in salt solution introduced per rectum, *H*, or in form of suppositories, *D* and *G*, all failed to have any appreciable effect on the excretion of urine. At no time during the patient's stay was her fluid intake limited; she had free access to water and the fluid intake was such as her sense of thirst dictated. These tests show that pituitary gland substance in liquid form, introduced subcutaneously, had a striking effect on urine excretion, decreasing it to normal if sufficient gland substance was used, while other ways of giving gland substance had a negligible effect. The action of gland substance, absorbed from the subcutaneous tissue, was temporary, and better effects were obtained by more frequent dosage than by larger doses given at longer intervals. As we shall see later, the quite long-continued use of pituitary substance in this case had no demonstrable effect on the bone defects.

Two determinations of basal metabolism were made on this patient for us by Miss E. H. Tompkins in the hospital respiration laboratory. It would seem from her reports that no great departure of basal metabolism from the average normal was present. Apparently there was a moderate decrease in activity of metabolism.

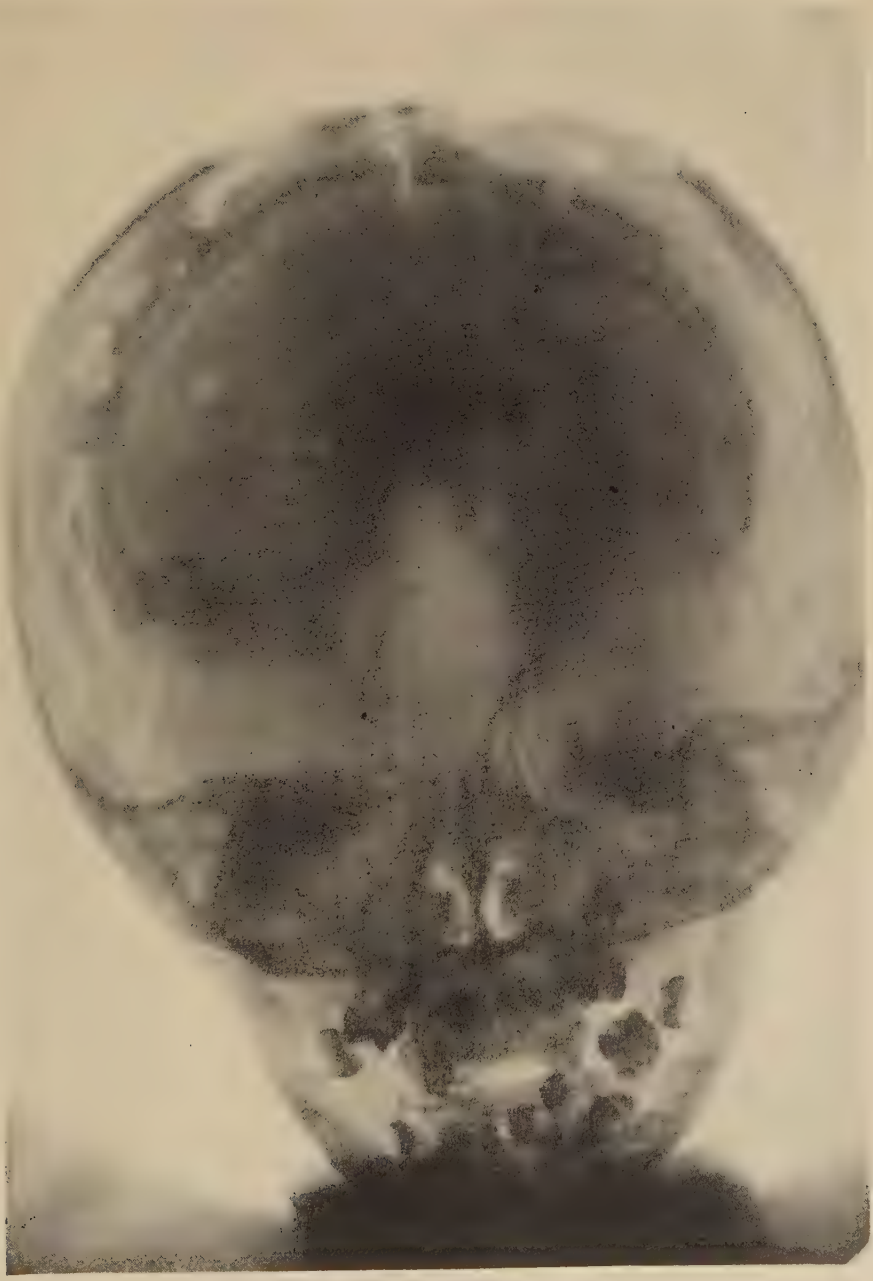

FIG. 3. ROENTGENOGRAM OF SKULL.
Showing Bone Defects. Frontal View. (See p. 396.)

FIG. 4. ROENTGENOGRAM OF SKULL.
Showing Bone Defect, Lateral View. (See p. 396.)

This would be in complete accord with our usual findings in adults with disturbances of pituitary function.

The most remarkable feature in this case was the truly extraordinary picture revealed by roentgen rays. A number of plates were

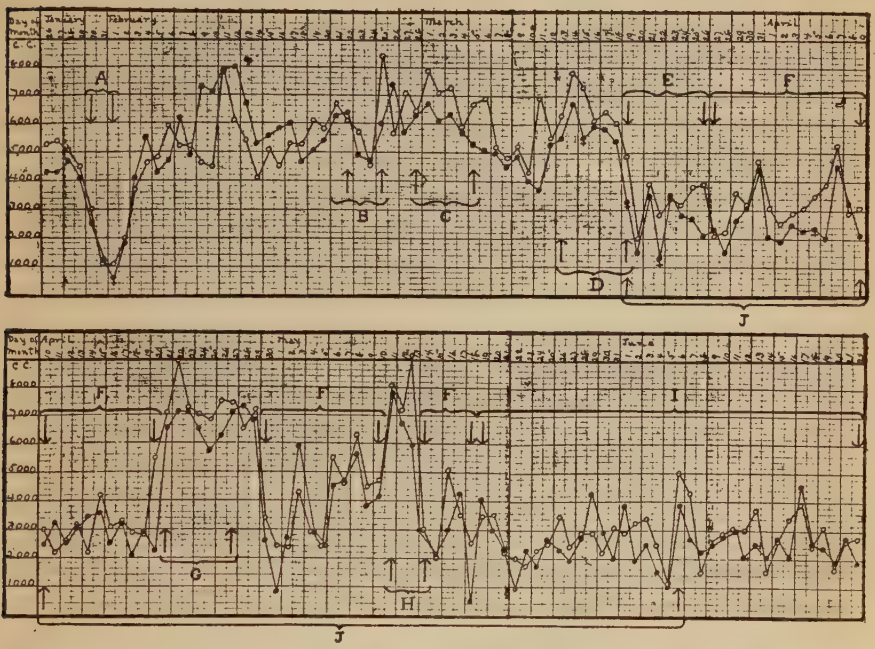

CHART III. SHOWING FLUID INTAKE, URINARY OUTPUT FOR EACH TWENTY-FOUR HOURS. LETTERS AND ARROWS REFER TO PITUITARY SUBSTANCE GIVEN IN VARIOUS WAYS AS INDICATED BELOW.

A. Pituitrin, 4 drops subcutaneously three times a day. Began at 3 P. M. on 1/30 and stopped at 6 P. M. on 2/1. *B*. Dried pituitary gland, .1 gram three times a day in gum drops dissolved in the mouth. Began at 8 A. M. on 2/21 and stopped at 8 A. M. on 2/25. *C*. Dried pituitary gland, .1 gram three times a day in gum drops dissolved in the mouth. Began at 8 A. M. 2/28 and stopped at 4 P. M. on 3/5. *D*. Powdered pituitary gland, .1 gram in suppositories four times a day. Began at 12 noon 3/13 and stopped at 4 P. M. 3/19. *E*. Pituitrin, .25 c.c. subcutaneously three times a day. Began at 8:45 P. M. on 3/19 and stopped at 8 P. M. on 3/26. *F*. Pituitrin, .05 c.c. subcutaneously twice a day. Began at 10 A. M. 3/27 and stopped at 6 P. M. on 4/20. Began again at 12:35 4/30 and stopped at 10 A. M. 5/10. Began again at 6 P. M. 5/14 and stopped at 10 A. M. 5/18. *G*. Pituitrin suppositories containing 1 c.c. of pituitrin four times a day. Began at 9:20 A. M. 4/21 and stopped at 8 P. M. 4/27. *H*. 2 c.c. pituitrin in 200 c.c. of salt solution per rectum twice a day. Began at 6 P. M. 5/10 and stopped at 10 A. M. 5/14. *I*. Pituitrin .075 c.c. subcutaneously twice a day. Began at 6 P. M. 5/18 and stopped on discharge 6/22. *J*. Powdered pituitary extract by mouth, .1 gram four times a day. Began at 8:45 P. M. on 3/19 and stopped at 12 noon 6/6.

made during the six months' observation; several times stereoscopic plates were taken. Rather than give a description of these individual plates a composite description of the group will be attempted. Fortunately a year before admission (February 22, 1917) she came

to the hospital and skull plates were made. These showed at that time a similar, though slightly less extensive, process.

The striking thing in a complete roentgen-ray study of the skeleton was the very extensive defects in the skull bones, slight but similar changes in the flat bones of the pelvis, and a quite normal appearance and normal stage of ossification and development of all other bones in the body. The defects in the skull caused an appearance which can be best described by comparing them to the irregular holes in a bit of moth-eaten flannel or the appearance of a pasteboard box gnawed full of holes by mice. (See Figs. 3 and 4.)

As seen in the lateral view, Fig. 4, the most extensive defects are in the anterior half of the skull. Of the frontal bone, particularly the lateral portions, only irregular rather narrow septa of bone are left between the large islands of entire bone disappearance. In a similar way the orbital plates of the frontal bone have largely disappeared, so that there is little bony support remaining for the eyeballs. In the parietal bones there are extensive defects in the vertex portions, whereas in the lateral portions of the parietal bones there are only a few round defects, measuring from 1 to 2 cm. in diameter. In the occipital bone only three small circular defects are present.

Viewed in the antero-posterior direction, Fig. 3, the very extensive defects in the frontal bones are very evident, as is also the irregularity in the orbits of the eye. The best idea of the character of the skull defects is obtained from stereoscopic plates, from which it is perfectly clear that the defects represent a complete loss of all bone substance capable of throwing any distinct shadow characteristic of bone. The variations in density at different places in the bones when seen in the ordinary plates are due to the fact that in some places there are defects on the two sides of the skull in line with each other, whereas in other places the defect on one side of the skull is opposite to a place where intact bone remains in the opposite bone. Almost everywhere the margins of the defects are sharply cut, as if the line of demarcation between no bone and fairly normal bone or normal bone is a very sharp one. Only here and there do the edges show a ragged appearance, indicating points where small projecting portions of bone remain intact. This picture may be due to the fact that the inner table at this point remains and the outer table has been dissolved or destroyed or vice versa. At certain points

in the stereoscopic plates it is evident that there are small round defects or cavities in the substance of the bone with a thin inner and outer table still intact, and at one point in the lateral view the thinner and outer tables can be seen projecting as faint shadows beyond the general substance of the bone. The character of the round defects of small size seems to be similar to the character of the large irregular defects. About none of these defects does the surrounding bone show any thickening or other evidence of proliferation, and where the defects do not exist the structure of the bone seems entirely normal. The sella turcica seems somewhat enlarged and slightly flattened, and in the stereoscopic view it looks as if there is a defect in the base of the skull very close to, if not continuous with, the sella turcica.

Plates taken at different times show very slight variations in the picture. On February 22, 1917, the defects were evidently less numerous and less extensive than on January 30, 1918. The last plates taken, those of June 10, 1918, after six months' stay in the hospital under treatment with various forms of pituitary substance, show no change, apparently, of progression or retrogression in the defects as contrasted with the picture of January, 1918. All the other bones in the skeleton except the pelvic bones show no change whatsoever. In this bone in the lower half of the ilium there is slight irregular rarefaction suggesting small incomplete defects roughly circular in character, similar to what is seen in the skull, only very much less marked, and in the anterior portion of the ischium near the acetabulum there is also slight irregularity in the density suggesting loss of substance.

Discussion. A careful search of the literature revealed but one report of a similar condition. Schüller in the *Fortschritte auf der Gebiete der Roentgenstrahlen*, 1915–16, XXIII, 12, under the title "*Ueber eigenartige Schädeldefekte in Jugendalter*," describes two cases observed by him in Vienna. In these *x*-rays of the skull show the same condition as described in my case. His description is as follows:

Case I. "Boy of sixteen years. Four years ago a running ear began on the left. Since then the left side has been slightly deaf. Three months ago the patient noticed that his left eye was more prominent than the right. Since then a slight inflammation of the left eye has been present. There has never been any headache, dizziness, vomiting, or decreased

vision. Recently there has been double vision in looking to the side, affecting mostly distant objects. They stand either parallel or leaning toward each other. In January, 1913, the patient was 137.5 cm. high and weighed 39.5 kilos. Panniculus adiposus richly developed. Cheeks fat. On both sides of the neck above the clavicle fatty tumors. Also in the thorax there is much fat and the abdomen is fatty. Arms and legs also fatty. No abnormal findings in the internal organs. No symptoms of tuberculosis or syphilis. The genitals are small and completely infantile. The right lobe of the thyroid slightly larger than the left but not abnormal. Skull dolichocephalic. Forehead short and somewhat narrow. Over the left eyebrow the skull is somewhat sensitive. The face is asymmetrical. The left half appears prominent and seems as if swollen. The left eye projects about 8 mm. beyond the right. Movements of the left eyeball unaffected. Nystagmus looking to the side. In the fundus of the left eye the veins have dilated without pulsation. The fundus is normal.

"Skull is roomy; 4 mm. thick. At different places in roentgen-ray plates the left half of the skull shows clearing of the bone shadow corresponding to extensive ulceration of the skull. The greatest defect is in the region of the left parietal bone near the mid-line. This defect shows an irregular, nearly square form; diameter about 3 to 5 cm. From the posterior lower corner of this defect goes a narrow horn-like, half-moon, curved process. The edges of the defect are sharp. The central part of the defect appears brighter than the periphery. Further defects are found in the region of the left frontal bone and in the region of the occiput. The walls of the left orbit do not appear changed as compared to the right. The sella is small. The dorsum sellæ are intact. Reflexes all normal. There can be no doubt that the combination of dystrophia adiposo-genitalis and protrusion of the eye can be explained on the assumption of a tumor at the base of the brain. Other things suggest pressure. The suggestion is made that the tumor is an angioma of the dura or of the skull bone."

Case II. "Four-year-old girl who when 1½ years old had whooping cough. When two years old suddenly developed left-sided exophthalmos. At that time the physician who saw the child demonstrated a defect in the skull roof. Some months later suddenly a right-sided exophthalmos appeared. In October, 1913, the child was small and slender. Skin and mucous membrane pale. Microscopic and Wassermann study of the blood was negative. Internal organs and neurological examination was unimportant. No glandular swelling. No remains of any previous rickets. Intelligence of the child well developed. Markedly increased thirst and polyuria up to eight liters daily. The child's head is of normal size and oval shape. The growth of hair is very sparse. Extensive portions of the scalp

are free of hair. Both sides show high-grade exophthalmos. Vision amounts to at least 6/20. On both sides there is temporal pallor of the optic nerve. On palpation the skull shows several defects of different extent. They are partly oval; partly oblong. The edges of the defects are sharp and firm. Where the defects exist one feels the pulsations of the brain, but the membranous covering of the defect does not bulge but seems slightly sunken; *x*-ray of the skull shows very plainly the defects. They appear both in the transverse and sagittal picture as an entirely peculiar, map-like spotting of the *x*-ray shadow. Only a relatively small part of the skull shadow corresponds to the normal bone thickness. Within very extensive regions one sees different sized and differently formed clear places. These are partly light gray and in part completely lack the ordinary deepening or shadow of bone. The former correspond to skull defects without any on the opposite side. The latter are defects which overlie defects on the opposite side. The edges of the defects are completely sharp. When the defects appear in profile the edges have a funnel form so that the defect in the lamina externa is greater than the lamina interna. The skull between the defects seems entirely normal. Also in the region of the base of the skull extensive defects are recognized. The well-known contour of the upper edge of the orbit is completely lacking on both sides. The orbital roof appears almost completely eroded. The sella turcica is markedly changed. Only the dorsum sella is present. The anterior part of the floor of the sella is greatly deepened. The destruction of the roof of the orbit explains the exophthalmos. In January, 1914, the symptoms had not changed. The defects in the skull plainly were smaller. *X*-rays of the pelvis taken at this time showed a round defect about the size of a five-crown piece in the right ilium and also a spindle-like thickening in the upper part of the right femur (healed fracture). The explanation of this case is very difficult. The history makes it plain that it is not a congenital, but an acquired disease of the skeleton. The clinical observation shows that the process is capable of regression. We can, therefore, make a presumptive diagnosis of anomaly of the skeleton as the result of disease of the hypophysis."

In some cases of muscular dystrophy, as pointed out by Janney and his coworkers (1) and by others, atrophic changes occur in the skull bones somewhat similar to those found in my case and the two cases of Schüller. In muscular dystrophy, however, the bone changes are, by far, less extensive. It is of particular interest that Janney and his associates are maintaining in this paper the thesis that muscular dystrophy is closely associated with disturbance in glands of internal secretion, and in one of

their cases there was evidence of a causative connection between dyspituitarism and muscular dystrophy.

The only condition in which I have seen any resemblance to the bone picture of the case here reported, and that only a partial one, is multiple myeloma. With this condition the skull and other flat bones often show in the roentgen ray scattered round or oval defects due to tumor growth. In these cases I have never seen any large irregular bone defects. In multiple myeloma palpation usually reveals a nodule where the roentgen ray shows the larger bone defects, so the resemblance is but a superficial one.

Syphilis might cause somewhat similar bone defects from gumma formation. Schufeldt (2) pictures a skull with extensive destruction of bone from a negro of twenty-four without further statement than that "eventually the fact became known to me that this negro had died from tertiary syphilis." Adami and Nicholls (3) give figures of a somewhat similar skull labeled "periostitis with destructive inflammation (osteoporosis) affecting the frontal and temporal bones, supposedly due to syphilis." In syphilis, however, breaking down of the gumma and later scar formation in the scalp is to be expected. In my case no evidence exists of any previous local imflammatory condition and the patient's blood Wassermann was negative.

Cranio-tabes in rickets occasionally shows thinning and defects in the skull bones, but there was nothing in our case very suggestive of rickets. Osteoporosis congenita presents some similarity, but this is an ill-defined clinical group whose nature is too little understood to throw any light on this patient, and I have found no cases described under this heading very similar to the case here reported.

That a disturbance in the secretion of the pituitary gland is responsible for the defects in the flat bones in this case is an hypothesis that has considerable support. The coexistence of diabetes insipidus controlled by subcutaneous injection of pituitary substance is strong evidence of a disturbed pituitary function. Motzfeldt (4) and others have shown by clinical and experimental observations that there is a relation between diabetes insipidus and deficient pituitary function, as Motzfeldt expresses it, "lowered activity of the posterior lobe of the pituitary body." In the only two cases similar to mine that I can find reported (5) evidence of pituitary disturbance was noted, in one an adiposo-genital dystrophy, in the

other diabetes insipidus as in my case. In such an unusual disturbance as is represented by the bony defects in these three cases it could hardly be coincidence that there existed in each evidence of disturbance in the function of the pituitary gland. Rather does it seem highly probable that the bony defects are caused in some way by changes in the pituitary gland, changes as to whose exact nature we have no evidence from the study of these cases.

Summary. A case is described where in a girl of five there occurred the symptom complex of very extensive defects in the skull bones, exophthalmos, and diabetes insipidus. Only two other cases of this condition could be found in the literature. Diabetes insipidus suggests that the symptom complex is due to a disturbance of pituitary function. Both of the other two reported cases showed evidence of disturbed pituitary function. In the case here reported pituitary extract controlled the polyuria when given subcutaneously. Other methods of introducing pituitary substance had no effect on the polyuria. No method of giving pituitary substance had any effect on the bone defects or exophthalmos.

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SPECULATIONS CONCERNING THE RELATIONSHIP OF CANCER, DIABETES MELLITUS, AND TUBERCULOSIS TO AUTONOMIC ATAXIA AND ENDOCRINE DISORDERS

WITH SOME OF THE FACTS OF OBSERVATION ON WHICH THEY ARE BASED

By Solomon Solis Cohen, Philadelphia, Pa.

AUTONOMIC disorders, their heredity, their complexity, and their variability, have not escaped the study of Osler. Reference need only be made to his papers upon angioneurotic edema and the connection of the erythema group of skin diseases with visceral crises and other neurovascular disturbances. (1)

The same group of phenomena—viewed, however, from a different angle—arrested the writer's attention in the first year of his practice, and has been the subject of observation and speculation ever since. The first case was seen in 1884, recorded and demonstrated in 1885; the second was exhibited in Bartholow's clinic in 1886. Partial reports, clinical and theoretical, have been published from 1890 on (2); but, so far as the theories are concerned, have received, at most, only qualified approval in the general court of professional opinion.

Sir William's remark in a discussion at the meeting of the Association of American Physicians in 1908, that the writer's conception of the scope of *vasomotor ataxia* is too extended—making it, in fact, a "scoop net, including pretty nearly everything worth studying," is perhaps the most generous of the dissentient criticisms, and in the discussion of Raynaud's disease in his own article in "Modern Medicine,"[1] he adopts and defines the term within the limits he deems appropriate.

This criticism has induced the writer to justify, in part at least, the original broad conception, by an amendment of the name for

[1] 1st Edition, VI, 627, Philadelphia and New York, 1909.

the more extended groups of disorders; and he now uses the term *Ataxia Autonomica*, in place of the restricted *Ataxia Vasomotoria*, which properly belongs to a subgroup—wide, indeed, but not so wide as the range of phenomena at first described thereunder.

It is true that these phenomena of imbalance, as originally described, are most strikingly manifested in the vasomotor domain; but they are by no means confined thereto, or even to the circulatory system. They may affect any system, any organ, any anatomical region, almost any tissue. They do not constitute disease; but they are the substratum of many diseases and disorders. Possibly 3 to 5 per cent of the human race will show some trace of this fundamental, constitutional, and usually hereditary abnormality, if scrutinizingly examined and tested. In many, it remains a mere liability; in others, under the incidence of various exciting and determining causes, it gives rise to more or less severe and persistent disorder—always with a tendency to paroxysmal or critical disturbances.

Eppinger and Hess (3), in their descriptions of "Vagotonia" and "Sympathicotonia," have merely applied other names to some of the varied pictures of disorder published many years earlier by the writer and—in avowed sequence—by Hans Herz (4).

Their studies do, indeed, help to clarify our notions of the underlying pathological-physiological mechanisms; and their pharmacological tests may, at times, aid in diagnosis; but they have set up a false viewpoint.

The communication to the Pan-American Medical Congress of 1893, in which the writer summarized ten years' clinical studies, divided the phenomena, from the viewpoint of the clinic, into three classes, characterized (1) chiefly by abnormal dilatations of vessels (*angioectasic*, Herz); (2) chiefly by abnormal constrictions of vessels (*angiospastic*, Herz); (3) by a varied commingling of abnormal dilatations and abnormal constrictions (*mixed*); and it was there pointed out that the third class is by far the most common.

Theoretically, it was admitted that one can picture an exclusively angioectasic condition, and certain cases of Graves's disorder come near to manifesting this; or one can picture mentally an exclusively angiospastic condition—and Raynaud's disorder frequently approaches this. But there were described a number of cases in which

Raynaud's phenomena and Graves's phenomena (including goiter, tachycardia, and certain eyelid symptoms) were found in the same patient at different times, and even at the same time. Other cases were narrated in which one set of phenomena were found in some degree continuously, and the other set paroxysmally. Consequently, since neither paralysis nor spasm, stimulation nor inhibition, can be alleged with certainty as the cause of constriction or dilatation at any given time, in vessels under the control of opposing innervations (and the same thing is to be said of other functions—e.g., secretion or peristalsis), and since neither condition is in any instance continuously exclusive—however much it may predominate—the more general term of *ataxia* was adopted to indicate a condition of malgovernment, inco-ordinate activity, imbalance, or precarious balance. The mistake was made, however, of attaching to the general condition the name of one only of the systems affected, since the whole domain of the autonomic-sympathetic-endocrine complexus is involved; and this is, indeed, a "scoop net," which does not include "everything worth studying," but does include much.

Now, in arbitrarily separating the complex, variable, multiform and multiregional phenomena of this vast domain into two sharply contrasted classes, depending upon hypertonus of one or the other of the two great divisions of the vegetative or visceral (Gaskell) or involuntary (Gaskell) or autonomic (Langley) nerve system—the cranio-sacral and the thoracico-lumbar, termed by German writers the autonomic and the sympathetic, by French writers the parasympathetic and sympathetic—the nomenclature of Eppinger and Hess conforms to a beautiful physiological theory, rather than to the actual facts of observation. Pure cases of "vagotonia" and "sympathicotonia," according to the descriptions given, are so rare that the writer in the course of more than thirty years' study of cases of this order has met none that he could so classify.

Even from this viewpoint, then, that of the mechanism of the phenomena, we are forced back upon the conception, not of a predominant hypertonus of one or other of two opposing systems of visceral-vascular innervation, but of an imbalance or instability—a tendency to excessive reaction from slight cause—a want of *taxis*—of the system, considered (as it is by Langley and by Gaskell) as

a whole. To which may now be added explicitly—as hitherto implied—a similar conception of the great related system of glands of internal secretion.

We are thus moving in the region of greatest present-day obscurity. What was said twenty-six years ago may be repeated: Neither physiology nor pathology, neither physics nor chemistry, yet gives us the exact data upon which to base a scientific nomenclature; to distinguish causes, effects, concomitants, amid a complexus of obscure reactions; or even to attain other than a vague view of the fundamental factors concerned in these disturbances.

The term proposed as a clinical memorandum rather than a pathological description, but amended to show more clearly its scope, is therefore retained in the present communication.

In the paper of 1893 stress was laid upon the diverse manifestations of autonomic imbalance, not only in the same individual at various times, but also in the families and clans of which such individuals are members; and one family and clan was mentioned especially. To the paper of 1898 the same family and clan supplied new illustrations. Since then it has given many more.

Among the tendencies or ailments manifested by its various branches and members, cancer, diabetes mellitus, and tuberculosis were cited; and in many papers and discussions during a quarter of a century, some fundamental relationship of autonomic ataxia with cancer, with tuberculosis, and with diabetes has been affirmed, tlthough the nature of this relationship could not be indicated.

It has been shown, from the first, that to produce the paroxysms or the continuous manifestations of the group of disorders under discussion, three factors must co-operate:

1. The fundamental liability—that is, the autonomic instability or actual imbalance.

2. An excitant.

3. A local determinant.

The excitants have been shown to fall chiefly into five classes: (*a*) emotion, (*b*) fatigue, (*c*) noxæ (i.e., toxic substances, endogenous or exogenous), (*d*) thermal changes, (*e*) trauma. It is possible, however, that fatigue should be considered with noxæ—that its manifestations, in part at least, are due to fatigue-poisons.

In dealing with vicious circles it is hard to say which point is the

beginning; and this is especially true in regard to both the exogenous and the endogenous noxæ that may be concerned in the production of autonomic disorders. For example, in Graves's disorder there is frequently present an endogenous noxa, the toxic thyroid secretion; and this secretion induces various morbid autonomic reactions which figure in the complexus of symptoms. But whether that toxic secretion originates the whole autonomic disorder, or is—as the writer, among others, believes—merely a secondary result of perverted action of the thyroid gland dependent upon an original disturbance of the autonomic system—may fairly be termed an unsettled question.

As to *tuberculosis*, three views, at least, are possible: 1. That the autonomic disorders—including thyroid enlargement and certain eye-signs—so often seen in tuberculous subjects, are the results of a tuberculous toxemia, whether of bacterial or tissue origin. 2. That they are manifestations of susceptibility to tuberculosis. 3. That they are manifestations of a protective reaction.

Which is more likely to be correct? Reversing, for convenience of discussion, the natural order, the conclusions will be stated first—the evidence adduced later.

In the writer's opinion, at first, the second view seemed most plausible; but it has been gradually overshadowed, and now superseded, by the third; and this, indeed, has been frequently stated in discussions at medical meetings and in clinical lectures. The chief factor in bringing about this change of opinion has been the frequency with which marked autonomic disorders—or the physical manifestations described as indicating liability thereto, or positive responses, direct and reflex, to the mechanical and thermal tests laid down for the study of this class of subjects—have been found (1) in the immune members of tuberculous families and the immune families of tuberculous clans; (2) in the subjects of various forms of rapid, acute tuberculosis; (3) in the subjects of slight, chronic, or healed tuberculosis.

What is it that these have in common, and that is less manifest in the ordinary subjects of tuberculosis? Not tuberculous toxemia; not susceptibility; but immunity, or a furious, abortive effort to produce it.

As to *cancer*, it is an old clinical observation that whereas car-

cinoma and tuberculosis are rarely found in the same individual, they are not uncommonly found (*a*) in different members of one family; (*b*) in different families of the same clan; (*c*) in different generations of one line of descent—sometimes, indeed, almost regularly alternating.

Now, it has been found that in immune families of cancerous clans, and in immune members of cancerous families, the autonomic disorders are pronounced and varied; and this, as in the similar case of tuberculosis, is too frequently encountered to be mere coincidence.

If the liability to carcinoma is fundamentally related to the liability to tuberculosis, we have the same problem as to the true relationship of that liability with the autonomic disorders. Is it toxemia? Is it susceptibility? Is it immunity? And the answer is probably the same. The one that seems most plausible is immunity.

The conditions in *diabetes mellitus* are opposite—or perhaps the facts may be better expressed by saying that the relationship is inverse. The old teaching that diabetics are peculiarly prone to tuberculosis, and that it is a frequent cause of death among them, is not confirmed by more modern observation. On the contrary, the number of cases in which tuberculosis supervenes upon diabetes is far less, proportionately, than the number of cases of tuberculosis found among persons whose carbohydrate metabolism is not obviously disturbed—who, at all events, do not manifest glycosuria or glycuresis, either persistent or temporary.

What might be shown by a sufficiently extended study of blood-sugar in the subjects of tuberculosis, one cannot say in the absence of such a study; and it is not to be forgotten that many practitioners —the writer among them—consider it advisable to reduce the proportion of carbohydrates in the dietary of consumptives. Be this as it may, the number of tuberculous patients developing frank diabetes mellitus is less than the number of diabetics among the non-tuberculous—or, to speak with due reserve, among those in whom tuberculosis is not overtly manifest.

The relative infrequency—rarity is, perhaps, too strong a term—of tuberculosis and diabetes mellitus in the same individual is indeed such that when recently half a dozen persons so affected—four men and two women—were under the writer's care at one time, this focused his attention upon the subject sufficiently to induce a tenta-

tive presentation of his views in a discussion before the Association of American Physicians. (5)

But, as repeatedly stated, both diabetes mellitus and, if not diabetes insipidus, at least a high grade of polyuria, are relatively common in the families of those presenting evidences of autonomic imbalance. Not only this, but transient glycosuria, and, more frequently, recurrent polyuria, are found at one time or another in most of these subjects if they are kept under sufficiently close and persistent observation. The polyuria and glycosuria of Graves's disorder, and the ease with which glycosuria can be provoked by the administration of adrenalin in certain subjects of autonomic ataxia, need merely passing mention.

The relationship, then, appears to be distinctly one of susceptibility. Autonomic instability would seem to render one liable to transient or persistent lessening of carbohydrate tolerance.

It may be, however, that the provocation is the "other way round." Or it may be that the error of metabolism and the disorder of autonomic functions are simply parallel results of the same pathological condition, and that the primary lesion or functional perversion is to be sought in the endocrine system. We have again the same problem that is presented by the vicious thyroid circle in Graves's disorder; and the solution may be the same or different. Available data do not permit one to dogmatize.

Clinically, however, we have these obvious facts:

1. Persons of tuberculous lineage, but themselves immune, present varied autonomic and endocrine disorders.

2. Among such persons and their non-tuberculous relatives—even when the latter do not present sufficiently obvious signs of autonomic and endocrine disorder to seek medical advice concerning them—disturbances of carbohydrate metabolism are common.

3. The coincidence of frank diabetes mellitus and frank tuberculosis in one person is not, perhaps, rare; but it is relatively infrequent.

The inference that susceptibility to tuberculosis and insusceptibility to diabetes—and, conversely, immunity from tuberculosis and liability to diabetes—may depend, in a certain group of persons, upon factors clinically expressed by autonomic or autonomic-endocrine disorders, is suggested. It is by no means proved; but it seems to be worth consideration and study.

One form of the suggested relationship—for there are many possibilities—may crudely be outlined thus: An individual of a certain constitutional type—for the present we cannot get back of that—while accidentally subnormal, is invaded by tubercle bacilli. Yielding at first, he later develops certain factors of resistance; resulting, primarily or secondarily, in over-stimulation, sometimes exhaustion, and perhaps perverted activity here and there, in the nervous, motor, and secretory functions of organic (vegetative) life —that is to say, in the gangliated nerve system, in the circulatory apparatus, in the secretory glands, especially the thyroid and adrenal, and in the viscera. Either in his own person or that of his descendants, these endocrine and autonomic changes become organized into definite syndromes, or remain as a constitutional proneness, or liability, to a varied group of disturbances. Among such disturbances are decreased tolerance to carbohydrates and a tendency to the development of diabetes mellitus. Persons developing diabetes mellitus retain in large degree their inherited immunity against tuberculosis. Persons who fail to develop immunity from tuberculosis do not acquire, in like number, the special liability to carbohydrate intolerance or diabetes mellitus manifested by others of the same lineage.

It is not an insignificant fact—since we are dealing with phenomena of heredity spread over many generations and lines and not condensed as in the foregoing crude outline—that the Hebrew race is to a certain extent immune from tuberculosis, and prone to diabetes mellitus and endocrine and autonomic disorders in general. The immunity is not perfect; the liability is not exclusive. Environment, social status, the vicissitudes of individual life, etc., have much influence. But we are here viewing largely, and in outline only, a large subject, and this great historical example is not to be ignored.

It is true that the cause of the immunity may be very different from the cause of the liability, and that the relationship may be quite other than here suggested. We may be dealing with mere coincidences. The liability to autonomic disorders may plausibly be attributed to the emotional strains of centuries of persecution—and it is not without its compensating aspects which need not here be elaborated. The immunity from tuberculosis may be an instance of survival of the most resistant, or of some other form of biological

adaptation. But whether these or other explanations that have been offered be true—and none is the whole truth—the facts remain; and the facts have bearing upon the subject of these speculations.

And now, as to the evidence: It would be impossible—and it is unnecessary—to detail here the great mass of cases and family histories collected in more than thirty years. Some have been published in full in previous communications, and no number can support an erroneous conclusion. But one may cite a few illustrations of the family and clan relationships referred to.

By clan is meant a group of families; by a family, the two generations of parent and child, or the three generations of parent, child, and grandchild. In a few instances great-grandchildren have been included.

In America it is not always easy to trace the varied relationships and connections of one's patients through several generations; and here, as everywhere, such tracings are exposed to the fallacies of coincidence and of ignorance. A man may not know whether or not his grandfather had cancer or migraine, which does not necessarily mean that the grandfather was exempt. Also, although one may find gout or asthma in several members of the paternal stock, it may be that this particular patient has acquired his affection independently, or inherits from the maternal line. This only means that one must not overstress the relationships found in any particular instance; it does not vitiate, but rather tends to increase the importance of, such positive evidence as can be gathered.

It so happens that in the case of two clans, which will be designated as *A* and *B* respectively, individuals of three generations of some of the families have been under the writer's personal observation, and there is more or less information to be obtained concerning five, or even six, generations.

Of *Clan C*, individuals of two generations have been under observation; or of three generations, if we count as belonging to this clan the children of a marriage in which all three strains—*A*, *B*, and *C*—commingle.

Of *Family Z*, two generations have been under observation. Nothing is known of the medical history of earlier generations.

All of these individuals, families, and clans have been in fair or

good circumstances, so that, except in one instance to be noted, our problem is not complicated by any question of privation or exposure. Nor have there been any dissipated or dissolute individuals among those reported; and there is no trace of any inheritance of lues or alcoholic degeneration.

Clan A is able to trace its pedigree on both sides for many generations; but for our purposes, the first to be cited[1] are Mr. A_1 and Mrs. A_1, born, one in England, the other in America, in the latter part of the eighteenth century. Of ancestry and relatives earlier than this we take but passing notice, since our knowledge of their medical history is too fragmentary to be of high value. On both sides, however, we can positively affirm a tendency to gout and to long life. It may or may not be significant that one of Mrs. A_1's paternal uncles died of "consumption," since this is said to have followed privation and exposure during his service in the "Continental" Army.

Of Mr. A_1 and Mrs. A_1 we know, medically, little; and that little is mostly negative. Both died in late middle life, one of cholera, the other of yellow fever.

Five of their children, whom we will call the second generation (A_2), have either been under observation in their old age, or their history is authenticated. These five individuals will be designated A^{I}_{2}, A^{II}_{2}, A^{III}_{2}, A^{IV}_{2}, and A^{V}_{2}, under which headings their respective families (children—A^{N}_{3}—and grandchildren—A^{N}_{4}) will be grouped and discussed together.

Family A^{I}_{2}. The first of this family to come under observation was a daughter fifteen years old, a member of generation A_3. Briefly, she was subject to attacks of transient blindness, not hysterical, followed by intense headache; burning flushes; erythematous outbreaks (scarlatiniform and morbiliform); erythema nodosum; urticaria; circumscript edema. The thyroid gland was palpable, but not enlarged. She is still subject to occasional severe headache and to sudden pain in the lower extremities, suggestive of angiospasm.

Her father (A^{I}_{2}) had married a member of Clan B of the contemporary generation. He died in his sixties of acute pneumonia, after having suffered for forty years of active life from repeated pulmonary hemorrhages attributed to "disease of one lung," possibly chronic fibroid tuberculosis.

[1] Arabic numerals below the line indicate generations of a clan or family. Roman numerals above the letter indicate families of a clan.

The other children of this family (generation A_3^I) likewise exhibit one or another form of autonomic disorder. One who, as a girl, was subject to profuse epistaxis occurring without apparent cause, but was otherwise healthy, has, within the past year, developed angiospasm of the lower extremities and distinct exophthalmic goiter. There is a record that twenty-five years ago she showed, upon testing, in addition to dermographism and factitious urticaria, that larval stage of Stellwag's sign—namely, excessive voluntary or involuntary retraction of the upper eyelid provoked by convergence and fixation of the eyeball—to which the writer has repeatedly called attention, and to which some of his friends and pupils have given his name.

A brother (A_3^I) of the preceding patient was for many years subject to ophthalmic migraine, bronchial asthma, and gastric crises corresponding with periods of lithuria and oxaluria. The thyroid gland was slightly enlarged, and he exhibited what the writer has called the costal fringe; namely, a network of teliangiectases following the outline of the costal arches. Later he developed severe gastric hemorrhage attributed to ulcer, but from which he recovered without operation. He then began to suffer from anginoid symptoms, and died in his fifties, apparently in an attack of angina pectoris. One of his children (generation A_4^I) is beginning to show signs of *petit mal*, and is subject to transient ecchymoses without obvious cause. Another (A_4^I) was subject in early childhood to emotional crises of the alimentary tract and of the bladder.

A sister (A_3^I) shows but slight signs of autonomic disorder—recurrent, and sometimes giant, urticaria and tendency to syncope. But among her children (A_4^I) we find eczema, scarlatiniform erythema proceeding even to desquamation; pseudo-appendicitis; hay fever. One young woman of generation A_4^I, whose parent apparently escaped the family tendency by early death from acute endocarditis, recently developed a mild case of Graves's disorder. In generation A_5^1, of which the eldest member is seven years of age, there is as yet but one case of pronounced disorder—a girl with recurrent erythema.

Family A_2^{II}. In this family the head was gouty, and lived to a very old age, to die of broncho-pneumonia. He exhibited only leucoderma, but was always markedly intolerant of opium and chloral, and had but slight tolerance of quinine. Three of his children (generation A_3^{II}) likewise exhibit leucoderma. Of these, one was also subject to migraine until far advanced in life; and had severe bleeding hemorrhoids, relieved by operation. He had at times paroxysmal attacks of pain simulating gall stone. This patient is still vigorous in old age, but is subject to occasional attacks of vertigo, which apparently bear no relation to anything except fatigue.

His blood pressure is below the norm of his age, and his arteries do not give evidence of pathological change. Of his children (A_4^{II}), one has migraine and shows the eyelid sign the writer demonstrated in 1892 as the "hitch" or "interrupted descent," and which was, later, described by others. It appears to be a larval stage of Von Graefe's sign. Another child (A_4^{II}) has intestinal crises of varied types.

The second leucodermic (A_3^{II}) has a long history of chilblains, and was subject in youth to "severe bilious attacks," sometimes attended with syncope and cyanosis. They seemed to be provoked by slight indigestion, and always followed the eating of veal, until this was prohibited. An attack in later life was mistaken for appendicitis. They were, of course, intestinal, and possibly gall-duct or appendicular crises, and in all probability had an angioneurotic origin. He has bleeding hemorrhoids and suffers with migraine and occasional vertigo, but has reached his seventieth year in fair vigor.

The third leukodermic (A_3^{II}) was subject, as a child, to profuse epistaxis and had migraine until relieved by proper glassing in his twenty-fifth year. He had in youth repeated attacks of what seem from description to have been pseudo-appendicitis (angioneurotic edema of appendix). He is easily poisoned by veal or mushrooms, and now avoids both. He has been subject to slight anginal paroxysms and to unexplained attacks of polyuria, and has shown transient glycosuria. He has some tendency to obesity and must diet to avoid podagra. He had bleeding hemorrhoids, relieved by operation. In his sixtieth year he is hale and hearty, but still has hay fever and occasional vertigo. One of his children (A_4^{II}) has hay fever, and was subject as a child to widespread angioneurotic edema and to severe ecchymoses from slight knocks. Another (A_4^{II}) shows marked intolerance of quinine and salicylates.

A fourth brother (generation A_3^{II})had migraine in youth, and died in his forties of rapid diabetes mellitus. One of his children (A_4^{II}) has severe hay fever and persistent eczema. One of his grandchildren (A_5^{II}), aged nine years, shows a tendency to hay fever.

A sister (A_3^{II}) has had retinal hemorrhages, but is otherwise hearty and vigorous in advanced age. Another sister (A_3^{II}) had chorea, and was subject to repeated and profuse epistaxis and to repeated attacks of panaris. A third sister (A_3^{II}) is pathologically obese and is subject to circumscript edema. Her son (A_4^{II}) has severe hay fever and asthma. Finally, the youngest member of generation (A_3^{II}) has been subject since childhood to attacks of what is called "winter eczema," but is characterized by blueness and fissuring of the finger tips, and can be prevented by wearing woolen mittens.

Family A_2^{III}. The father died in his thirties of a pulmonary hemorrhage attributed to tuberculosis. The son (A_3^{III}) had chronic glaucoma and died in middle age of some intercurrent affection.

Family A_2^{IV}. The mother was gouty and died in her late seventies of what was called dysentery, but which appears from description to have been broncho-pneumonia coincident with a final attack of recurrent mucous enteritis. She had five children (A_3^{IV}). One, in his sixtieth year, had an unexplained attack of nasal hemorrhage which is said to have threatened death by repeated recurrence, but from which recovery ensued. There is no other information obtainable. One, in middle life, had an obscure affection of the autonomic system diagnosticated by one physician of international repute as Addison's disease, by another as Graves's disorder, and by a third, as neither. It was accompanied with transient glycosuria. Complete recovery ensued without diagnosis. Of the others, no significant information is obtainable. One of the grandchildren (A_4^{IV}) has eczema and hay fever; another has urticaria, and had what seems from description to have been intestinal hives, simulating appendicitis.

Family A_2^{V}. The mother had migraine, but lived until her sixtieth year in apparently robust health. She then developed hemorrhagic pulmonary tuberculosis, of which she died. Her son (A_3^{V}) had attacks of syncope leading to a mistaken diagnosis of "heart disease," and has had frequent paroxysms of renal colic, followed by the passage of uric acid gravel. No information is obtainable concerning later generations.

Families A_2^{VI} *and* A_2^{VII}. There were two other members of what has been called here the second generation (A_2) of this clan, both women. One, unmarried, was hale and hearty all her long life, and died in her nineties, of what was called dysentery. The other, married, died in her sixties, two years after operation upon a breast tumor called "cancer," and, presumably, of metastatic involvement. Detailed information concerning her children, grandchildren, and great-grandchildren cannot be obtained, but it may be positively affirmed that there has not yet developed among them any case of overt tuberculosis or cancer.

Summary: Among seven sons and daughters of a woman whose uncle's death from tuberculosis may or may not have been significant, there are three cases of pulmonary tuberculosis, all hemorrhagic, and one case of carcinoma; but no case of tuberculosis or carcinoma in any subsequent generation, up to, and including, the fifth. All these generations, however, and so far as information is obtainable, every family shows marked and persistent autonomic and endocrine disorders, and there is one case of diabetes mellitus in the third generation. The clan in general is gouty and long-lived.

Clan B. The ancestry is strongly gouty and neurotic on both sides. No

sufficiently definite information is obtainable concerning generation B_1 (contemporary with A_1).

A member of Family B_2^I married, as already stated, into Clan A, and became the mother of the family designated A_2^I. Under emotional shock she was subject to attacks of prostration with feeble and irregular action of the heart, and the urine at such times would contain albumin and blood-cells, and even casts. She was subject to angiospasm of the lower extremities; but lived in comparative vigor into her eighties, to die of bronchopneumonia.

One of her brothers (B_2^{II}) and one of her sisters (B_2^{III}) died of diabetes mellitus, the brother in youth, the sister in advanced age. One sister (B_2^{IV}) and two nieces (B_3^{II} and B_2^{III}) died of carcinoma. Several cousins (B_2^{II}) have exhibited Graves's disorder, diabetes, or carcinoma. In a family derived from another cousin, two sisters (B_3^X) have attacks of "dead fingers" and spontaneous ecchymoses, followed by pain simulating that of renal or ureteral calculus, or miscalled "sciatica"; and one of them also had desquamative erythema and visceral (intestinal) crisis. One has an enlarged thyroid gland without toxic symptoms. A third sister of this family (B_3^X) has eczema and migraine.

One of Mrs. A_2^I's brothers (B_2^V) died of pulmonary tuberculosis. Two of this brother's children (B_3^V) have had hemorrhagic pulmonary tuberculosis and have fully recovered. One of them has developed pathologic obesity and angioectases of the foot. The other has migraine, vertigo, and abdominal crises. A third member of this generation (B_3^V) was subjected by a surgeon of deservedly high repute to exploratory operation for recurrent colicky attacks, apparently caused by gallstones, but nothing was found. There was no recurrence of the attacks after operation. A fourth (B_3^V) is subject to vertigo and transient blindness. After one of these attacks a transient retinal edema was observed by a competent ophthalmologist. The blood pressure is moderately high (160 systolic), but there is no other evidence of organic change of any kind. His daughter (B_4^V) has had attacks of erythema with abdominal crises of various kinds, from all of which there has been recovery. His son (B_4^V) has had attacks of pseudo-appendicitis.

Summary: In a large group of gouty and long-lived families exhibiting very marked and varied signs of autonomic disorder, cases of tuberculosis, diabetes mellitus, and carcinoma are found in two generations; but so far as can be ascertained, without occurring in the same person. While carcinoma and diabetes mellitus recur with some frequency, tuberculosis is found in but one line; and although the father died, the two children affected (both hemorrhagically) recovered fully, and both, since recovery, show certain signs of autonomic imbalance and endocrine disturbance. Information, quite desirable,

is lacking, concerning the presence or absence of autonomic disturbances in the individuals affected with carcinoma and diabetes. Although a member of this clan married a tuberculous member of the preceding clan, none of her issue, or of their descendants to the fifth generation, has a history of overt tuberculosis or of carcinoma; while all show marked autonomic-endocrine disorder.

Clan C. The earliest generation to be observed is contemporary with A_2 and B_2, and will be called C_2.

The father of the only *Family* C_2 to come under observation exhibited nothing of significance for this study; but the mother is subject to migraine, and to recurrent giant urticaria, and is highly intolerant of quinine. She occasionally shows transient glycosuria. Her parents, aunts, and uncles are said to have been similarly affected, and her brothers, sisters, and cousins are said to exhibit, among them, nearly the whole gamut of autonomic disorder—Graves's syndrome, hay fever, asthma, visceral crises of various kinds, dead fingers, hemorrhages of various kinds (not fatal), "blood blisters," articular and periarticular swellings, mucous enteritis, erythema, eczema, etc.—as well as diabetes mellitus. Four of her children (C_3) have come under observation. All of them are intolerant of quinine. Two have had giant urticaria; one has migraine; one has hay fever; and one has shown, in addition, those peculiar phenomena in and about the joints sometimes called *hydrops articulorum* (*intermittens*) *nervosa* or *vasomotoria;* but which the writer has preferred to describe as angioneural arthroses and pararthroses (6).

The last-mentioned young woman married a member of family A_2^I, which, it may be recalled, was constituted by intermarriage between Clan A and Clan B. As might be expected, all of the five children of this marriage have pronounced autonomic disorders. Angioneurotic edema, recurrent epistaxis, pseudo-appendicitis, chilblains (so-called), erythromelalgia, hay fever, migraine, syncopal attacks, dead fingers, precordial pain simulating angina pectoris, mucous enteritis, vertiginous spells, scarlatiniform erythema, are among the phenomena thus far observed in one or the other at one or another time. So far as can be learned, there has been no tuberculosis in any recent generation of Clan C, and no history of tuberculosis is known, so far back as the ancestry is traceable.

Summary: A group of families in which no tuberculosis or carcinoma is known to exist within recent generations, exhibits most marked and varied autonomic and endocrine disorders and has several instances of diabetes mellitus. The children of a marriage between one of this clan and one of the issue of the intermarriage between the two preceding clans show many and marked autonomic disturbances, but thus far neither tuberculosis, carcinoma, nor diabetes mellitus. If the thesis of this paper is correct, they should all be im-

mune from tuberculosis and carcinoma, but diabetes mellitus—or, at least, glycosuria—is to be expected in one or more of them, if not prevented by proper regime.

Family Z. Of the first generation to come under observation (Z_1), only two members are known personally, but the history of the others is authentic. One died of pulmonary tuberculosis. One has recovered from tuberculosis. One died of carcinoma. Two have cardiovascular disturbances, which from description were at first functional, with tendency to critical manifestations, and are now organic. One has a tendency to syncopal attacks; has manifested anginoid symptoms; and has suffered, and in great part recovered from, an affection of the lower extremities variously diagnosticated by various good observers—Raynaud's disease, recurrent angiospasm, thromboangeitis obliterans, and endarteritis obliterans being among the conditions suggested. A child of this patient (Z_2) has had an abdominal crisis of the type termed by the writer "hives of the appendix." Another child (Z_2) was operated upon for appendicitis, but nothing abnormal found. So far as one can learn, there has been no diabetes mellitus in this family or its ancestry or near branches.

Summary: Of six brothers and sisters, two have tuberculosis and one has carcinoma. These did not marry. The others are immune from tuberculosis and carcinoma, but show marked vasomotor disorders, eventuating in vascular lesions. Of their children information is at hand of two only, in one family. Both of these show angioneuroses.

The foregoing—which, with their positive data and their lacunæ, are typical of the material at hand—are but a few of the family and clan histories that could be cited. Nor has even the complete history attainable of Clan A and Clan B been given—many of the collateral branches exhibiting phenomena quite similar to those described. Nor has the catalogue of symptoms, crises, or syndromes been exhausted.

But nothing is to be gained by merely multiplying instances. If coincidence is the explanation, a thousand coincidences will prove no more, and no less, than one. But the phenomena are too distinct, the relationships too marked, to be thus put aside.

The facts seem beyond gainsaying, that diabetes mellitus or other form of carbohydrate intolerance is frequent among the subjects of frank disorder or feeble taxis of the vegetative nerve-system (*autonomic ataxia*) and among their relatives—while tuberculosis is relatively infrequent among diabetics and is rarely found in overt

form in those who exhibit pronounced symptoms or syndromes of autonomic disorder, although found in their ancestry and perhaps among near relatives. Carcinoma, too, seems to bear some relationship to autonomic disorders similar to that of tuberculosis.

It may also be noted in passing that gout[2] is frequent in the family histories, and this cannot fail to remind those who are still willing to take account of persistent professional and lay traditions, that gout has been considered protective against tuberculosis and carcinoma and to be a predisposing cause of diabetes mellitus.

The writer has, therefore, felt justified in reassuring patients who —presenting marked autonomic disorders, and aware of tendencies to tuberculosis or carcinoma in their families or lineage—have expressed a fear of developing cancer or consumption, by telling them that they are protected; that they are, in all probability, suffering from an "excess of protection." Thus far, the assurance of immunity, the prediction of safety, has not proved false in any known instance; that is to say, when the individual could be kept under observation or in touch.

The assumption on which that assurance is based may be an error—but the observation is submitted to a competent jury for criticism, and, it is hoped, further study.

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[2] The relationship between gout and autonomic-endocrine disorder is close—but its discussion would lengthen this paper unduly.

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BLUISH DISCOLORATION OF THE UMBILICUS AS A DIAGNOSTIC SIGN WHERE RUPTURED EXTRAUTERINE PREGNANCY EXISTS

By Thomas S. Cullen, M.D., Baltimore, Md.

ON March 21, 1918, there entered the Church Home and Infirmary a thin, wiry woman (C.H.I., No. 18,744) who looked to be nearly sixty years of age, but who was actually only thirty-eight. She was the mother of seven children. For three weeks she had had pain in the right lower abdomen with intermittent attacks of abdominal distention. One week after the onset of the trouble the umbilical region suddenly became bluish black (Plate), although there had been no injury whatsoever in this region. Pelvic examination was very unsatisfactory on account of the marked abdominal distention.

Operation March 27, 1918. With the patient asleep the uterus was found to be slightly enlarged. To the right of the uterus was a freely movable mass about 8 cm. long by 5 cm. broad. I was instantly reminded of a case reported by Dr. Joseph Ransohoff of Cincinnati and referred to at length on page 307 of my book on "Diseases of the Umbilicus." Dr. Ransohoff was called to see a man of fifty-three who presented a somewhat obscure abdominal condition. This was associated with jaundice of the umbilicus and of the umbilical region. At operation rupture of the common duct was found and the abdomen contained a large quantity of free bile. The abdominal wall was especially thin at the umbilicus, and the absorption of bile was clearly seen at this point. Bearing Dr. Ransohoff's case in mind I dictated the following note prior to opening the abdomen: "The bluish black appearance of the navel unassociated with any history of injury, together with the mass to the right of the uterus, makes the diagnosis of extrauterine pregnancy relatively certain, although the patient has not missed any period and although there has been no uterine bleeding."

On opening the abdomen I found it filled with dark blood, and attached to the fimbriated end of the right tube was an extrauterine pregnancy.

BLUISH DISCOLORATION OF THE UMBILICUS ASSOCIATED WITH A RUPTURED EXTRA-UTERINE PREGNANCY.

This picture was obtained at operation three weeks after the first symptoms developed. The umbilicus itself has now turned a light green; above it the tissue has a faint bluish tinge; below the umbilicus the blue is marked.

It was possible to remove this without sacrificing the tube. The patient made a good recovery and was discharged April 16, 1918.

In the Plate Max Brödel has given us the appearance of the umbilicus at operation. The umbilicus itself is of a greenish hue. Above the navel is a faint bluish tinge, below the umbilicus the bluish appearance is more intense.

The bluish coloration gradually diminished in intensity during the patient's sojourn in the hospital prior to operation, and disappeared completely within a few days after operation. The gradual change in color that took place in the umbilical region reminded one strikingly of the changes in color that occur in a black eye resulting from a blow.

I record this case in order that subsequent ruptured extrauterine pregnancies may be examined for this sign. Whether it will prove to be of common occurrence or very rare, I cannot say, but we shall naturally expect it only where there is free blood in the abdomen and shall probably be more likely to encounter it in thin individuals.

NOTE ON STRYCHNINE TETANUS

By Arthur R. Cushny, M.D.,

Materia Medica Laboratory, University of Edinburgh

In 1905 Sherrington (1) pointed out that the inhibition of antagonistic muscles which occurs in normal reflex movements is absent in the tetanic movement under strychnine; here both antagonists contract together, and the resultant movement depends upon their relative strength and leverage. Strychnine is generally said to change the inhibitory effect to a motor one through its action in the spinal cord, and this reversal of action has been extended to the vasomotor function by Bayliss' (2) observation that stimulation of the depressor nerve under strychnine causes a rise of pressure instead of the normal fall. Further analyses of the phenomenon by Sherrington (3) and by Owen and Sherrington (4), while abundantly confirming his previous observations, have not served to elucidate the nature of the change in spinal function.

It is difficult to reconcile this change with a number of old observations that under strychnine weak and slowly acting stimuli may cause a normal reflex movement in the frog, while a strong stimulus throws the animal into typical tetanus.

I have frequently demonstrated this simultaneous presence of tetanic and normal reflexes in the frog in the following experiment. The frog's brain having been pithed, wires from a secondary coil are attached to one foot; the frog is then suspended from a standard, and, after the normal reflex has been shown for rapid secondary shocks of varying strengths, strychnine hydrochloride, 0.05 mg., is injected into the anterior lymph sac, and the observations are repeated after time has been allowed for absorption.

In the unpoisoned frog a series of weak electric shocks passed through the foot induces a feeble movement confined to the tarso-crural joint, and as the strength of shock is increased, the movement becomes stronger and soon involves the knee as well as the ankle joint; finally the hip also is flexed as the current increases. As still

stronger shocks are applied a further spread of movement to the other limbs and the trunk follows, but in every case it is of ordinary reflex character, and the contraction of one set of muscles is seen to be accompanied by relaxation of their antagonists.

After strychnine, if the same procedure is followed, it is found that a weaker series of shocks causes the first feeble movements; the threshold for stimuli is lower. And as the strength of shock is increased the same extension of the movement is seen, in each case the stimulation threshold being reduced by strychnine; so that, for example, a stimulus which in the unpoisoned frog only sufficed to cause a feeble movement of the foot, now causes complete flexion of the knee and partial flexion of the hip. Apart from this change of threshold the reflex movement is identical with that in the unpoisoned animal, contraction of flexors being accompanied by relaxation of their antagonists as usual.

But as the strength of stimulus is further increased, a point is reached at which a completely new movement follows—the animal passes into tetanus, with simultaneous contraction of antagonistic muscles; the movement loses its purposive character, and the foot, instead of being withdrawn from the stimulus, is thrust towards it. The response to irritation thus depends entirely on the strength of stimulus, and below a certain point the reflex movement is indistinguishable in character from the normal, while above that point the phenomenon is that described as tetanus and reversal. By alternately using strong and weak stimulation, one can induce an alternation of typical ordinary reflexes and of tetanic spasms with complete absence of inhibitory relaxation of antagonists. It is thus difficult to conceive of strychnine having altered the cord so that it is no longer capable of emitting inhibitory impulses, for this kind of response follows only on strong stimulation, while weaker shocks are followed by normal inhibitory (and contraction) discharges.

An example may elucidate the change.

Experiment I. A frog with pithed brain had fine copper wires from the secondary coil twisted round the longest and the shortest toes of the right hind foot, while the left leg was strung up out of the way.

With the coils at 18 cm. distance a series of shocks lasting one-half second caused barely perceptible movement of the foot at the ankle joint. At 17.5 cm., weak movement at ankle. At 17 cm., movement of ankle

and knee. At 16.5 cm., good contraction at ankle and knee, and slight flexion at hip. At 16 cm., complete flexion at ankle and knee, incomplete at hip. At 15 cm., complete flexion at ankle, knee, and hip.

After $\frac{1}{20}$ mg. strychnine hydrochloride had been injected into the anterior lymph sac: Stimulation at 22 cm. distance, minimal movement of foot. At 21.5 cm., fair reflex movement of ankle and knee. At 20.5 cm., flexion of ankle, knee, and hip. At 18 cm., no normal reflex, but complete tetanus of the whole body.

Very often, as the strength of shock was increased, the reflex movement became more extensive, as in this experiment, but when the current was sufficient to cause full flexion of the ankle, knee, and hip, the movement began as a simple reflex, but was interrupted by tetanus.

When tetanus has been induced and has passed off, it cannot be renewed by a stimulus until after an interval for the recovery from fatigue of some part of the arc. During this period of exhaustion, stimulation of a strength which was sufficient previously to elicit a normal reflex, fails to cause any movement or is followed by a less active reflex than before. As the interval lengthens between the tetanus and the renewed stimulation with weak shocks, the effects of the latter improve until they are equal to those observed before the tetanus.

Tetanus thus fatigues the reflex arc and renders it less capable of renewed tetanus. It also fatigues the mechanism involved in the normal reflex movement from weak stimulation.

After a period of rest the normal reflex movement under strychnine can generally be elicited by weaker shocks than after a period of stimulation. And the greater the number of normal reflexes elicited in a given period, the weaker the response becomes. The arc concerned in the production of the ordinary reflex movement under strychnine is fatigued in the same way as in the unpoisoned animal, and in fact seems more readily exhausted. When the cord is thus fatigued by a series of normal responses, it is also fatigued for tetanus. This can be shown by two methods of observation. In the first a strength of stimulus is chosen which, after a period of rest, induces tetanus, and series of shocks are given at short regular intervals. The first series causes tetanus, the second a weak normal reflex, the succeeding series fairly strong normal reflexes, and these

may be continued indefinitely. If, now, one period of stimulation is omitted, the next in order is followed, not by a normal reflex, but by tetanus, and if the stimulation series is renewed at the former intervals, the effect again is normal reflex movements.

Experiment II. Frog prepared as in Experiment I. $\frac{1}{20}$ mg. strychnine. Coil distance 10.7 cm.

4h. 2m. Stimulation causes tetanus.
4h. 2m. 15s. Stimulation causes weak normal reflex.
2m. 15s.–4m. Stimulation every fifteen seconds gives normal reflex.
4m.–5m. 30s. Stimulation every thirty seconds gives normal reflex.
5m. 30s.–6m. 30s. No stimulation.
6m. 30s. Stimulation causes tetanus.
7m.–13m. Stimulation every thirty seconds—normal reflex.

Here a stimulus which was sufficient to cause tetanus after a period of rest was unable to do so when the cord was kept in a partial state of fatigue by a series of normal reflex movements.

Conversely, if the intervals between the stimulations are kept equal, and the strength is that necessary to elicit strong normal reflex movements, it is found that a stimulus sufficient to cause tetanus after a period of rest may be substituted for the ordinary stimulation without any tetanus following.

Experiment III. Frog with pithed brain received $\frac{1}{20}$ mg. strychnine hydrochloride, and was suspended as usual. Stimulation at 10 cm. gave strong co-ordinated reflex movement. At 7 cm., tetanus. Stimulation at 10 cm. every ten seconds for three minutes gave ordinary reflex. Then a stimulation at 7 cm. gave no tetanus, but ordinary reflex. After an interval of three minutes, during which no stimulation was given, a short series of shocks at 7 cm. again caused tetanus.

Thus under strychnine in the frog two different responses may be made to peripheral irritation—a reflex movement differing from the normal only in the lowered threshold, or a tetanic contraction differing from it in the absence of inhibition of antagonists. These two forms of response must have one part of their path in common, for fatigue from repetition of one of them impairs the other. This common path extends along the afferent path as far as the first synapse in the cord, which may be the point at which fatigue is developed.

Under strychnine in sufficient doses to cause tetanic spasm from strong peripheral stimulation, the normal reflex path remains unaffected except for a lowering of the threshold: there is no reversal when weak but efficient stimulation is employed.

Strychnine tetanus with reversal is thus a condition superimposed on the normal reflex and independent of it. It does not, however, appear to be an entirely new form of response developed under strychnine. In the normal frog, it is true, there is no analogous movement, so far as I have seen. But in mammals and man the sudden start caused by an unexpected sound or touch appears similar in character, though shorter in duration. Here the movement is occasioned by an external stimulus and is tetanic in nature, there being no co-ordinated inhibition of antagonistic muscles, but the general movement being determined by the relative power of flexors and extensors. The strychnine tetanus thus has its analogue not in the normal reflex movement, but in this powerful and incoordinated spasm of all the muscles. And strychnine appears to change this "start" reflex only by lowering its threshold of excitability. In normal persons a start is caused only by a very sudden and very powerful stimulus, often a sound or an unexpected touch. Strychnine lowers the threshold so that feebler stimuli induce the "start" reflex, and it is of longer duration.

Thus under strychnine the threshold is reduced not only for the ordinary co-ordinated reflex, but also for the "start" reflex. And the change in the latter may overtake that in the co-ordinated reflex, so that unless carefully graduated stimuli are used, the response may be invariably a tetanus, i.e., an exaggerated "start" reflex.

It is thus unnecessary to assume, as has been done, that strychnine changes the ordinary co-ordinated reflex, not only in quantity, but also qualitatively, by inducing a reversal of inhibition into contraction. Strychnine tetanus is merely a quantitative change of the "start" reflex which occurs under normal conditions.

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DYSTONIA MUSCULORUM DEFORMANS

WITH A DISCUSSION BASED ON THE STUDY OF TWO CASES

By Theodore Diller, M.D., Pittsburgh, Pa.

IN a paper on this same subject published by Dr. George J. Wright and myself a few years ago[1] we used the following language:

"The essential condition of dystonia musculorum is the peculiar torsion-like tonic and clonic condition of the muscles which alone ought to stamp the disease clinically; the picture presented then by the individual case would vary according to the function of the muscle groups involved. . . . We wish to lay especial emphasis on the peculiar character of the muscle involvement, which shows a somewhat stable or constant condition of tonicity, varying in intensity and with marked tendency to torsion and further complicated by movements of a clonic type. Voluntary movements are possible, but performed as though there were conflict of muscle groups. . . . Movements are neither those of tremor, nor chorea, nor tic, nor athetoid movement, although somewhat suggestive of all of them."

This quotation gives, I believe, in brief form pretty well, not only my own conception of this condition, but that of the majority of writers who have described it. There are doubtless cases in which the movements vary and which are less typical than those described by us.

It was in 1911 that Oppenheim first described and called attention to this condition, and at the time of the publication of our paper we were able to find altogether nineteen different reports referring to this condition, eight of them being by American writers. While Collins in 1911 objected to bestowing a new name on an old condition, Spiller, to whose attention Oppenheim's paper had been drawn, regarded the description as proper for a case which he had had under observation, variously diagnosed as tic and Huntingdon's

[1] *J. Nerv. & Ment. Dis.*, April, 1916.

chorea—unsatisfactorily to him—and at once recognized it as belonging to the group described by Oppenheim.

A good many of these cases were recorded by various observers as hysteria. However, one can hardly see how this diagnosis could be well supported in view of the fact that dystonia appears in childhood and is progressive, or at least stationary in character. Oppenheim inclines to the view that dystonia is organic in character, despite the fact that definite signs of organic disease were not found in any of the cases recorded and the single autopsy was negative.

Dystonia musculorum usually appears in childhood, is progressive, and chronic in character. In most cases the clonic-tonic spasms affect chiefly the muscles of the thigh and pelvis and the lower extremities. But cases are recorded in which the disease began in the upper extremities, and in some cases it was for a time confined to one extremity. It would appear that the Hebrew is especially prone to the disease. No cases of recovery are recorded.

It occurs to me on the basis of the reports and in consideration of case to be reported, we can feel confident that this disease or condition is on an organic basis, despite the fact that this case seen by me and those reported are to a degree subject to suggestion. There is more likeness in this respect, as well as in other respects, to paralysis agitans, a disease which begins slowly and insidiously and is often confined to one member for a long time, the movements in which are much affected by the emotions, although the disease is evidently upon an organic basis. Jelliffe's suggestion that the seat of dystonia may be in some portion of the cerebello-thalamo-cortical arc is worthy of consideration in view of Hunt's recent studies of paralysis agitans, in which he finds degeneration in the cells of the striate body.

Before reporting my case, I shall, for the sake of those who have not seen reports of this condition, insert a short summary of the case briefly reported by Wright and myself.

Case I. Hebrew man, aged thirty-two years, with normal mentality. He is affected with peculiar movements of both arms, shoulders, and head, which are neither those of tremor, chorea, tic, nor athetoid movement and which are like convulsive movements which the patient is trying to control. The movements are tonic, antagonistic groups of muscles being contracted at the same time, and they are affected with clonic torsion-

like movements. By a strong effort the patient can pick up objects such as a key or pencil. One arm is affected much more than the other. There is no involvement of the lower extremities or pelvis. The gait is normal and there are no sensory changes. These movements began very slowly and insidiously before the patient was fourteen. He is unable to state just when they did begin.

The additional case I have to report is as follows:

Case II. Patient is a girl, aged seventeen years, one of ten children, all well except patient. Father was killed in an accident; mother living and well. There is no evidence of any hereditary nervous disease in the family.

Patient was born naturally without unusual incident, and seemed to grow and develop quite normally until she was two years old, at which time she was talking and walking. At this time she was seized with a convulsion which was prolonged something like half an hour. Her fingers were clenched tightly and her arms and legs drawn up, while her eyes rolled toward the ceiling. She was stiff all over, and unconscious. Then during the next two months she suffered five or six similar attacks; during this time the patient was in bed much prostrated by illness of some sort, which was characterized by fever and weakness. Her mother states that in all attacks the child was unconscious; and she estimates that various attacks lasted from five to ten minutes each.

Up to the age of nine years the child was free from convulsive seizures, after which they reappeared, and for the space of six months she was subject to them at the rate of about two a month—attacks of precisely the same character as those described. Then she was free from attacks until the age of fifteen, when she was seized with a severe convulsion which lasted half an hour. Since then she has had no other.

The patient suffers from peculiar movements which began when she was two years old. These movements are attended with spasm-like condition of the legs which prevents her from walking and which affects her arms to some extent, although much less than the legs. She gets about from place to place by creeping, crawling, twisting, and squirming in a way that is difficult to describe.

These movements are always present during the daytime and become exaggerated when she is excited in any way. They are absent during sleep. Despite the movements the child is able to feed herself. The mother regards her as mentally normal. The child is extremely anxious to live and very desirous of being cured. She fears her mother may die and then no one will take an interest in her.

On my first observation of the patient she was in bed at the Mercy

Hospital. Superficial observation led me to suppose I was dealing with a case of chorea; but this notion was soon dispelled when I considered the character of the movements, which were really not those of chorea, but rather those of contraction, partial relaxation, torsion, and twisting—differing from the regular flail-like movements of chorea; then, too, of course, the history that the movements had existed since childhood afforded another argument against chorea. Articulation was defective and suggestive of cleft palate speech. Upon my second observation I found the child in her own home, sitting in a rocking chair, legs extended outward and feet in the form of talipes equinus varus, the great toes extended. The trunk and arms were to some extent affected. Speech was irregular and halting; but it was evident that the child was intelligent and had ideas which she wished to communicate. In short, the movements affected the whole body, the muscles of the lower extremities and pelvic girdle being most affected.

When one's hand is placed on the legs and thighs it is noticed that all the muscles are in constant state of hypertonus, and that superimposed upon this, so to speak, are clonic contractions, at rather short but irregular intervals, of large groups of muscles. There is constant irregular but not rhythmical movement of the whole trunk and legs, which is neither choreiform nor athetoid, nor tremulous, nor of the character of tic. These tonic-clonic contractions greatly interfere with movement and the patient cannot walk because of them, although, as stated before, she can creep and crawl in a fashion and manage to get up and down stairs. On account of the spasms, knee-jerks cannot be taken.

The same condition affects the arms, although to much less extent. The patient is able to do much more with her arms than with the legs. From time to time there are irregular movements about the face; and the speech indicates that there are movements affecting the muscles of phonation. Patient seems quite well mentally. Pupils react to light normally, also to accommodation.

If this case be allowed as one of dystonia musculorum, with what are we dealing? A symptom or a disease? Is it functional or organic?

Typical cases of tortipelvis with a "dromedary gait," etc., are striking clinical pictures which when once seen can scarcely be forgotten; but the fundamental thing is rather the character of the movements themselves. If we admit dystonia with torsion spasm, we must be prepared for diversity in the clinical picture; although right here there is danger of adding still further confusion

in the classification of the hyperkinesias by mistaken interpretations. Oppenheim insisted on a close analogy of symptoms, and in fact discarded other reported cases, particularly those by Ziehen. But until the mechanism of dystonia is better understood we are hardly warranted in limiting our conception too narrowly. Dystonia is the symptom rather than the disease. The convulsive seizures which have characterized my second case and which with febrile reaction ushered in the beginning of the movements, confirms me in the view which Wright and I expressed of this condition, viz., that it is in all probability organic in character. Hunt, after a close study of six cases, holds the same view. Thus far there has been but one autopsy report (by Ziehen), which was negative; and when one attempts to postulate an anatomical basis for this condition, one is forced to think of a combination of lesions rather than a single lesion, and variations in the degree and location of the lesion may account for the different symptomatology. Important work on the basal ganglia has been done by Madame Vogt, Wilson and Alzheimer, Dunlap and Hunt, and on the cerebellum by Thomas, Bolk, Weissenberg, and Mills, which has emphasized the importance of the extra-pyramidal mechanisms and their relationship to tremor, tonus, eumetria, and anatomatic and associated movements. In the light of this work older criteria of what constitutes an organic disease are, therefore, too narrow. Aside from purely pyramidal affections, disturbances of tone are seen, for example, in the lesions involving the cerebello-rubro-spinal, the cerebello-thalamo-cortical, and the lenticulo-rubro-spinal mechanisms, not forgetting Foerster's work on atonic diplegia in which the frontal cortex is involved. In dystonia one thinks, therefore, of the phylogenetically older subcortical centers. In my second case, the fact that the general intelligence of the patient is so good is argument in favor of ruling out higher cortical centers as seat of the disease, at the same time arguing for sub-cortical center as seat of the lesion. Dystonia has certain resemblances to athetosis, but ordinarily should be rather easily differentiated, although there are probably some transition forms which render a satisfactory distinction very difficult indeed. Paraplegic forms of dystonia have been described, and for a time some cases have shown only monoplegic or hemilateral involvement. All this increases one's conviction that the disease is organic, that

the anatomical basis is not strictly focal, and that besides the pure forms of dystonia there is a great likelihood of mixed types. Taking into consideration the fact that the disease occurs in childhood and early youth, the date of the latest development reported occurring at seventeen, that three of Ziehen's cases occurred in brothers and sisters, and that most of the reported cases have been in Hebrews, the possibility of an abiotrophy is suggested. One wishes for an autopsy studied according to modern methods and especially in the light of work already done in somewhat similar conditions.

OXYCEPHALY AND EXOPHTHALMOS

By George Dock, M.D., St. Louis, Mo.

OXYCEPHALY is a definite and sometimes striking anatomical condition, with painful and disabling results in many cases, but it has only recently found a place in text books. Original contributions are numerous, but we find no description in Allbutt's "System" (second edition; the word is used in connection with the skull of an idiot) or in Osler's "Modern Medicine." As might be expected, there is an adequate account in the eighth edition of Osler's "Practice" (1912), also in Tyson and Fussell's "Practice" (1914), and in Barker's "Monographic Medicine." Most case reports are in ophthalmological periodicals; very few in internal medical, neurological, or pediatric literature. The early stages are likely to be seen by general practitioners and pediatricians, and should be sought out by them in order to add to the knowledge of those stages. I was fortunate enough to see a patient in a medical service who, while presenting a characteristic skull deformity, for reasons made clear by the illustrations might easily have failed of recognition.

The case was interesting to me especially on account of its relations to exophthalmos in negroes. I have often pointed out in clinical work negroes with exophthalmos, but without myopia, arteriosclerosis, or Graves' disease, and without visible deformity of the skull or tumors of the orbit. I tried to get someone interested in the orbital details in negro skulls, but so far without success. Since seeing this case I have examined a collection of negro skulls in the museum of my friend, Doctor R. J. Terry, Professor of Anatomy in the Washington University School of Medicine. I could find no skull with the orbital conditions of oxycephaly, but there seemed to be more than the Caucasian proportion with the fronto-sphenoidal process of the malar curved back. This might explain some cases

of negroes with prominent eyes. This view is furthered by the brother of the patient referred to, who is reported here briefly as Case II.

The cases illustrate in brief: Possible heredity (father); first child female, normal skull; second child male, no oxycephaly as to vault, but exophthalmos; third child, female, oxycephaly, exophthalmos, increased intracranial pressure, decompression operation; relief of symptoms.

Case I. M. H., Colored, female, seventeen, single, domestic, applied for treatment at the Medical Out-patient Department of the Washington University School of Medicine, September 18, 1918.

Diagnosis. Congenital malformation of skull; keratitis, chronic; blindness partial.

Chief Complaint. Bulging eyes; heart beats too fast.

I saw the patient in the Out-patient Department. The nervousness and tachycardia were marked, but the absence of goiter and the peculiar eyes led me to suggest that she be sent into the wards for study. The patient was admitted to the hospital October 18, 1918.

Complaint. Sick stomach; general weakness; nervousness; prominent eyes.

Family History. Father dead; said to have had prominent eyes. Mother living and well; no signs of cranial disease. (G.D.) Sister aged twenty-five, skull 19 cm. long, 15 cm. wide, Hertel 18, width 97. Brother, see below, Case II.

Past History. Measles at five and whooping cough at the same time; was very ill. No scarlet fever, diphtheria, pneumonia, nor typhoid. Chills and fever at thirteen. Has had pains in head, arms, shoulders, and knees for the last ten years, especially during changes in weather. Tonsils were removed (?) at eight years. Rapid heart since tenth year; no edema, no dyspnea. First menses at thirteen, always regular. Denies venereal disease. Wassermann negative with three antigens. Up to one year ago worked as domestic. Has never been able to work hard because of weakness. Eats regularly; appetite good. Best weight 100 pounds, January, 1918. Present illness began about the age of ten or twelve, when she noticed weakness on slight exertion. At same time noticed heart fluttering and would become very nervous; "trembles all over." All her life easily scared, but worse since onset of present illness. Has never been really well since tonsils were removed. Shape of head not noticed by family. Eyes began bulging at ten years; spot on left eye began at eleven years; had "sore eyes" at the time. Both eyes have been sensitive since then; light causes lacrymation; eyes

FIG. 1. CASE I, WITH THE USUAL HAIR ARRANGEMENT.

FIG. 2. CASE I, WITH THE USUAL HAIR ARRANGEMENT.

FIG. 3. CASE I, WITH HEAD SHAVED.

FIG. 4. CASE I, WITH HEAD SHAVED.

It is Easy to Exaggerate the "Tower" Appearance by Tilting the Head, but I have Selected Natural Poses.

Fig. 5. Case I, Roentgenogram of Skull.

are painful at times; has headache and vertigo; sweats easily; bowels constipated. No urinary symptoms. No night sweats; sleeps well.

Physical examination. The patient, like the rest of her family, is a chocolate-colored Negro with woolly hair, of small and slender frame, fairly well nourished. The intelligence is good for race and age. There is no pain, dyspnea, or cyanosis. Skin warm, dry, and elastic.

Head. No abnormal depressions or elevations; the root of the nose is low; there is slight prognathism.

Eyes: Marked exophthalmos; right pupil measures 5 mm.; left is small and irregular; both react promptly to light and accommodation. Left cornea has milky patch 5 mm. in diameter which covers portion of pupil. Tension of bulbs normal, no nystagmus. Vision right eye apparently normal; counts fingers with left eye inaccurately at close range. Convergence very poor in left eye. No definite von Graefe. Small strip of sclera seen above pupil when patient looks downward. Only slight wrinkling of forehead on looking up.

Nose and ears negative.

Mouth: Tongue protrudes in mid line. Teeth in good condition; two middle upper incisors irregular.

No abnormal pulsations in neck. No enlarged glands. Thyroid not palpable. Pharynx clear, uvula absent; arch high, sharply dome-shaped. Tonsils show scars, both attached to anterior pillars. Crypts well marked. No exudate.

Heart and lungs negative. Blood pressure 120–80.

Extremities—Upper: Reflexes present, no palpable glands. No tremor of fingers with hands extended. Lower: Knee kicks present, no ankle clonus or Babinski.

Blood: Hemoglobin 90; red blood corpuscles 4,900,000; leucocytes 7200.

Urine negative for albumin and sugar. Phenosulphonephthalein: first hour 40 per cent, second hour 12 per cent, total 52 per cent.

Examination of eyes by Dr. Dock, November 4, 1918. Hertel exophthalmometer shows 30 on right, 30 on left. Eyes wide apart; distance 105 (usual figures by Hertel 18–22; distance about 97 for age and race). Pupils react to light and accommodation. Upper lids reach almost middle horizontal line, follow eyes down without spasm. On fixing straight ahead upper lids cover cornea about 2 mm., lower on right; sclera below visible 4 mm.; lower lids move imperfectly. Convergence good, but left eye unsteady. Referred to Ophthalmological Department.

Pulse has thus far ranged from 60 to 80; temperature 97° to 99° F. Complains of heart beating too fast when she wakes up in the night; feels heart beating, but no tachycardia on examination.

Abstract of examination of eyes by Dr. Shahan, November 4, 1918.
"Diagnosis: Exophthalmos, right and left.

"Without correction { O.D. vision = 20/19
O.S. vision = fingers

"Ophthalmoscopic examination: O.D. media clear, fundus normal. H. about 2+D. Disk and vessels normal. O.S. large scar. Field O.D. normal. Exophthalmos probably due to cranial deformity such as occurs in premature closure of sutures or later in rickets, lues, etc. Greater wing of sphenoid probably forms posterior instead of outer boundary of orbit. Possibility of partial hydrocephalus should be considered."

November 8, 1918. Complains of heart making her nervous. Heart rate 90, varies from 60 to 90, somewhat irregular at times. No murmurs.

Up to this time the peculiar shape of head had not been recognized. The thick and wiry hair made measurements difficult, but the following were noted:

Head, anterio-posterior	15.5;	sister	19
Head, lateral	14.1 cm.	sister	15
Malar prominences	11 cm.	apart	
Ears, just above	13 cm.		
Height from external auditory canal to level of vertex	13.9		

No sign of rickets in wrists, costal cartilages, or ankles.

November 9, 1919. Demonstrated in clinical lecture as case of oxycephaly with exophthalmos as result of skull deformity. Differentiation from exophthalmic goiter and tumors of orbit. Oxycephaly not obvious, but shown in skiagram.

The (stereoscopic) skiagrams were made by my colleague, Dr. Sherwood Moore, to whom I am indebted for the following notes: "The skull is thin generally and especially in the frontal regions, and shows marked 'convolutional atrophy' throughout, especially in the frontal and occipital regions. The upper frontal region is high in proportion to the rest of the skull. The blood-vessel sinuses are not conspicuous. The posterior fossa is deeper than normal; the tip of the left mastoid shows fewer cells than normal. The sella shows no abnormality. From the root of the anterior clinoid process to the external auditory canal the distance is 41 mm., or slightly shorter than normal. The angle of the roof of the orbit approaches the vertical. The accessory sinuses are small. There are no frontal sinuses. The face is negative."

I measured the skiagram in comparison with that of the skull of an epileptic negro girl of about the same age and size. The enlargement of the skiagram must be borne in mind.

	Oxycephaly	Epileptic
Root of nose to occipital protuberance	17.7	20
Superciliary ridge to occipital protuberance.	19.3	20.8
Height, occipital-superciliary line to vertex	11.7	9.8
Back of orbit to root of nose	4	5.5
Height of orbit	4	3.7

The patient left the hospital at this stage, but reported to the Surgical Out-patient Department, where my colleague, Dr. Ernest Sachs, saw the patient and obtained permission to trephine. I am indebted to Dr. Sachs for an opportunity of measuring the head after it was shaved for operation and of obtaining the later photographs.

Dec. 6, 1918. Head shaved, measurements:

	Cm.
Circumference of head	54.2
Greatest length	18.3
Inion-nasion	16.
Greatest width	14.5
Lower forehead, width	12.5
Zygoma, largest	11.8
Temples above tragus	14.0
Face, height from chin	17.6
Height of face to lips	13.1
Height of face to alveolus	12.0
External auditory canal to external orbital margin	.8
External auditory canal to middle closed eye R. 10, L. 9.	
External auditory canal to vertex	14
Hertel, R. 29; L. 30; width 105.	

The photographs show the height of the vertex, with a narrow vault, but no great prominence of the frontal region, as seen in so many cases of oxycephaly with exophthalmos.

Dr. Sachs made an operation for right temporal decompression November 21, 1918. His notes show: "The bone was extremely thin. A very large area was opened. The dura was under increased tension, but not so marked as in a similar case. Apparently no dilatation of the ventricle when punctured; 10–15 c.c. of fluid removed. Brain of normal color; vessels huge."

By December 6th the headache had ceased and had not returned up to the beginning of March, 1919.

Case II. I looked up the brother, but was unable, on account of racial idiosyncrasies, to get skiagrams and photographs. I got a few data as follows: Twenty-two years old; no abnormality of skull noted by family; eyes always large. Had had no symptoms, except sore eyes several years ago, leaving an opaque patch on right cornea, covering the pupil. Works when he feels disposed. He is about 5 feet 6 inches high, slender, but apparently in good physical condition.

The cranium is narrow but not notably deformed:

Greatest length	19.5
Greatest width	14.5
Zygoma, greatest width	13.5
Temples above tragus	13.5
Height, ext. auditory canal to vertex	14.0

Hertel, R. 30; L. 29; distance 102.

The forehead is smooth, the nose aquiline; the root not low; the eyes are very prominent; the lids show no abnormalities; do not droop like those of Case I. The chin is small and receding.

Other measurements could not be obtained. It seems certain, however, that in this case, without conspicuous deformity of the vault, the orbits are much altered in the characteristic oxycephalic way, a marked example of negro exophthalmos, and a suggestion of the field of investigation presented by that race.

In the following brief study I have reflected the literature, almost all of which I have read in the originals, without attempting monographic completeness. As the references can all be found in the Index Medicus and in the articles cited, I have not added a bibliography. Schüller's "Rontgen-Diagnostik der Erkrankungen des Kopfes," 1912, translation by F. J. Stocking, Mosby, 1918, is useful, as is also the "American Encyclopedia of Ophthalmology."

Terminology. The variety of names given to the condition results partly from the attempt at etymological accuracy in a series of changes presenting transition forms. I prefer the term chosen by Sir William Osler, because it is the one most frequently used, is short and euphonious, and as indicative as any one term can be. The name is not intended as a description, but as a label. The skulls really do not suggest towers, steeples, etc. The effort to apply

"tower" for one variety and "steeple" for another breaks down under the numerous intermediate forms. Measurements, photographs, and skiagrams are necessary for conveying an accurate idea of shape, no matter how refined the terminology may be. "Turricephaly," "turritum caput," and the dozen or so other words should all be abandoned, but the several names given to various other types of skulls have a proper place in pathology and anthropology.

Oxycephaly may be defined as Osler does—"a cranial deformity associated with exophthalmos and impairment of vision." That the eye lesions are not always present does not lessen the value of the definition in a clinical sense. For more exact indications, as in case reports, one can speak of oxycephaly with exophthalmos, papillitis, optic atrophy, or blindness, as the case may require.

Shapes of the Skulls. The most constant and characteristic abnormality of the skull, by the usual methods of examination, is the increased height. This is most often found in the frontal, but may be in the parietal region. The cranium is always wide in proportion to the length, and the cranial cavity may be almost spherical, as in the case of Flournoy. Many other variations occur, such as pointed vault, suggesting a Gothic arch. Or the skull may look as if squeezed from before backward, but may be long, and even have a saddle-like depression of the vault though with high forehead (Krauss). There may be symmetry of the halves, but often there are striking exceptions, as in the case of Krauss, with oxycephaly, plagiocephaly, dolicocephaly, macrocephaly on the right and microcephaly on the left side. Many local details have been noted, as thickenings or depressions along the course of the sutures, one-sided flattening or depression of malars, enlargement in any portion, swelling or dome-like elevations (Dizeur) in the frontal region, flattening of the superciliary ridges, relative or absolute smallness of the occipital region, shortened fronto-sphenoidal process of the malars with rolling out of the outer wall of the orbit and shortening of the latter, or variations in the distance from the external auditory canals to the outer edges of the orbits as compared to the normal or to each other. Mather's case showed a bony prominence in the occipital region the size of a walnut. Like some others, the metopic suture was open. The base of the skull shows, perhaps, the most important

changes, but owing to the fact that skiagrams were not made until about 1907, the material is not as extensive as is desirable. The fossæ are usually deep and wide. In Paterson and Lovegrove's case the posterior fossa formed more than two-thirds of the base. The cribriform plate may be sloping downward, or funnel-shaped. The sella is often altered. It is sometimes short and deep and the middle fossa as low as the posterior, the "basilar lordosis" of Bertolotti. There may be a hollow space in front of it, looking not unlike the sella. Sometimes the sella stands out with unusual clearness (Fletcher), as in my Case I, and may be large. There may be asymmetry of the face, nose, upper or lower jaw. The exophthalmos is sometimes greater on one side. Anomalies of smell and taste occur as the result of local alterations of the base. In one case the odontoid process of the axis projected into the cranial cavity like a tumor. The sinuses and antra are usually small, but in Fenton's case (1915) the sphenoidal sinuses were large. Cleft palate, anterior and posterior, has been noted, but does not seem especially frequent. The orbits are always short in distinct cases of oxycephaly, the greater wings of the sphenoid pushed forward and sloping, the vertical diameter increased in front, the transverse often lessened, the cavities flattened in the posterior part. Prognathism is often noted.

Oxycephalics show other anomalies, but the statistics are hardly extensive enough to show whether these are more frequent than in people with normal skulls. Among the findings are syndactilism, polydactilism, small mouth, defective teeth, early caries of teeth, lack of last upper molars and other anomalies of teeth, high palate, congenital bilateral dislocation of radius, rudimentary concha, hallux valgus, genu valgum. Rare findings are persistent septo-labial ligament (Küttner), dermoid of the bridge of the nose, patent ductus arteriosus (Mather—autopsy at three weeks), hernia.

X-ray Examinations. The profile of the skull is well brought out in marked cases; in those not so marked—oxycéphalie larvée of Bertolotti—the changes in the orbits and base are diagnostic. From the fact that exophthalmos is sometimes present in skulls not notably deformed in the vault, it is more than probable that changes in the base can be discovered by *x*-ray examinations that would be missed without it. The atrophy of the inner tables, giving a mesh-like or webbed appearance, "digitate impressions," looked upon as evidence

of pressure by the convolutions, is in most cases very striking. It is often associated with hyperostosis, either between the impressions or in other parts of the skull, as the ethmoid and sphenoid. The vascular foramina are often enlarged, up to 1 cm. in a case of Strebel; the blood channels are often wide. Perforations of the skull, so-called auto-trephining, can be recognized in some cases, either in the parietal bones, where they may be large and symmetrical (Paterson and Lovegrove, 1900), or on the roof of the orbits. The teleological relation assigned them seems unwarranted.

Cause of Deformities. The modifications of the skull are due, in the first place, to premature closing of sutures, and this synostosis varies in seat and degree in different cases. The most frequent site is probably the sagittal suture, next the coronary and temporosphenoidal, parietal-sphenoidal, less frequently the lambdoid and parieto-occipital. Gratiolet's "law" will be recalled: In the higher races the sagittal, lambdoid, and coronary sutures close late. Pommerol, confirmed by Frédéric, showed early closing in negroes. With the early closure there may be compensatory enlargements so that the cranial capacity is often not small. Measurements of 1400–1500 c.c. are not unusual.

The cause of the early closure is still obscure, and it is almost certain that this obscurity is due largely to incomplete knowledge of the associated conditions. There is a suspicious agreement that syphilis is rare, though in few cases were accurate histories and serologic data available. Rickets is also denied by many observers, and admitted to be rare by many compilers, but found rather frequently by others. As Krauss points out, in many of the patients gross signs of rickets were absent, but there were suggestive records of late walking. Cohen reported a case as one of "rachitic pseudo-tower skull." Alcoholic and neuropathic histories in the parents are not especially numerous. Hereditary history is rare. Bedell reported the case of three members of a family affected. One had optic atrophy, another optic neuritis, the oldest was free from optic nerve lesions. The father was insane and a general paretic; the mother died of acute alcoholism. Microcephaly and thyreoaplasia were seen in one family. In one case father and mother were blood relations. In another case four generations gave histories of congenital dislocation of the lens and congenital heart disease. (Strebel, 1915.) Men-

ingitis or meningeal symptoms have been noted rather often. Meltzer suggested that a combination of rickets and hydrocephalus, as in serous meningitis, would give an impetus to synostosis, while more severe processes would lead to separation of bones. Trauma and struma have been suggested, but seem as unimportant as typhoid fever and influenza, which have been noted, seeing how many cases occur in very early life. In van Schevensteen's case there was a history of a fall at eighteen months, but a picture taken earlier showed a deformity already present. It is strange that Gudden's experiments have not been more fully tested. He believed that ligation of the carotids caused deformity of the skull without synostosis, while ligation of the jugular veins caused synostosis without deformities. Fletcher's idea of a definite (though unknown) morbid process, affecting the bones of the head more than others, is inviting, but not at present a definite gain. A remarkable fact is the greater incidence of oxycephaly in males. In the early days Friedenwald found that fifteen out of seventeen cases were in males. Dufour points out the larger heads in boys than girls. On the other hand cranial deformities in females must often be concealed by the hair.

The facts regarding closure of the cranial sutures are not as complete as can be desired. Bolk (1914) found some interesting results in examining the large collection of children's skulls in Amsterdam. Out of 1820 skulls coalescence was found both early and late—sometimes very late, as has long been assumed to be the rule. Early closure he found so often that he thinks it can hardly be considered abnormal. Unlike Frédéric, he often found two, three, or even four sutures obliterated. Out of the 1820 skulls at least 172 showed closure of the masto-occipital suture on one or both sides. Out of 725 skulls from three to six years old, 10 per cent showed such closed sutures, not due to ear disease. The sagittal suture in 47 out of 1820 cases showed complete closure in 19, and often before the seventh year. Rickets and syphilis were not thought to be present to a notable degree. The starting point of ossification was the obelion, which Bolk thought would not be likely if due to pathological causes. Recalling the early closure of the sutures in apes Bolk was inclined to look on the process in man as atavistic.

The time of occurrence of the ossification cannot be easily determined in living cases, but while synostosis may not appear

before late childhood, many cases are now on record in which deformity of skull, sometimes marked, was noted at or soon after birth, and with exophthalmos and optic nerve affections. Many patients began to show symptoms of optic nerve disease at about three years, or at the time the fontanels close. The earlier the symptoms the more severe they are likely to be. In Fenton's remarkable case the man of forty-seven gave a history of protrusion of the eye after forty. Few, if any, patients live to over fifty. (Fletcher.)

Bertolotti of Turin, in a number of suggestive articles,[1] looks upon oxycephaly as a lymphatic polyglandular dystrophy, with hypertrophy of Waldeyer's ring and lesions of the thyroid, sexual glands, and hypophysis. He quotes a striking description of the condition from Oribasius (fourth century—not sixteenth, as often stated in references to Bertolotti); insists on the adenoid facies of patients; signalizes the neglect of naso-pharyngeal examinations in them. While showing that the oxycephalic syndrome is the opposite to that of hydrocephalus, he believes that in many cases the diagnosis of rickets and hydrocephalus can be made in infancy, in which it is a sort of prodrome.

Symptoms. Besides the two main features, cranial deformity and symptoms of optic nerve disease, there are some others.

Exophthalmos is the most striking and is not uncommon. It may be absent in cases with great deformity, with high steeple head, and present with only slight cranial deformities. Patry found it in half of fifty-four cases. It is due directly to the shortening and flattening of the back of the orbit. "It is not due to myopia, as might be suspected from the frequent strabismus," but after appearing the exophthalmos may be increased by softening of the coats (Fenton). The exophthalmos is often extreme, but does not show the lid symptoms of exophthalmic goiter. On the contrary, many pictures show drooping lids, as in my own. Nystagmus is common, the mobility of the globes is often limited. Strabismus is frequent, usually divergent; in some cases it is the cause of bringing the patient to the ophthalmologist. The strabismic eyes often have poor vision from refractive errors. Keratitis, ectropion, lagophthalmos, and panophthalmitis have all been encountered. The eye changes

[1] See especially "Nouvelle Iconographie de la Salpêtrière," 1912, XXV, 1.

often give the patient an idiotic look, but the intelligence is rarely low, unless from early severe blindness. Even many totally blind oxycephalics have been able to acquire fair educations. In a five-year-old boy with oxycephaly, Herzog found a brain weighing 1240 grams, average for an adult. The deformity of the skull adds to the idiotic appearance, but, as an attendant remarked, "there are more queer-shaped heads in a blind asylum than in an idiot asylum." Convulsions and headache are frequent symptoms in the active stage of the disease or when the sight fails, and their occurrence should lead to a search for cranial deformities and optic nerve lesions, especially when vision is affected. Vomiting and loss of consciousness in such cases sometimes increase the suspicion of cerebral compression. Pain has been referred to the position of the ossified sutures. In a few cases, like my own, heart symptoms were present. Thus in a case reported by Stein (1914) the patient of nineteen had palpitation and dyspnea and was treated in a well-known hospital for heart disease and hysteria. The palpebral fissures were wide, but there was no von Graefe's sign. The heart was dilated.

Causes of Blindness. Some early observers thought the blindness so often found in oxycephaly was due to narrowing of the optic foramen, though there were others who from the beginning insisted upon other causes, such as meningitis and hydrocephalus. The latter, with deformities of the skull, had been described by William Mackenzie as early as 1866. This, especially internal hydrocephalus, sometimes in the third and fourth ventricles, has indeed been found, sometimes severe (Küttner). In some cases blindness occurs early and then disappears, which might easily be explained by temporary increase of pressure from disease. The paroxysmal course of the symptoms suggests changes of intracranial pressure. Friedenwald of Baltimore, in 1893, was the first to insist upon increased intracranial pressure. The blindness is due to post-neuritic atrophy, and the early stage of papillitis has often been observed. Beaumont (1909) thought the optic atrophy due to injury by bony distortion, and Behr (1910) claimed penetration of the carotid artery into the optic canal arresting the circulation of cerebrospinal fluid in the sheath and trunk of the optic nerve. In nine cases lumbar puncture gave no evidence of increased pressure. Schloffer (1913) also held

that there were causes other than increased intracranial pressure, especially local pressure on the optic nerve in its way to the orbit.

Fletcher introduced a variation by suggesting pressure by the growing brain, and this view has gained many adherents. That there is a disproportion between the skull and its contents is proved by the cases, becoming numerous, in which there was no evidence of distention by fluid in the cranium or spinal canal, but in which there was convolutional atrophy of the skull and actual crowding of the cranial cavity. In one of Schloffer's cases the brain swelled out of the operation opening to the size of a fist. Flournoy (1916–17) has shown some interesting facts proving the crowding of the brain in oxycephaly, such as narrow fissures, accessory convolutions, and molding of the cerebellum around the medulla. He thinks the effects of such pressure are not necessarily symmetrical on the skull; that the pressure may undergo temporary increase. This, with changes in the position of the convolutions, would account for the cases with digitate impressions much smaller than the width of convolutions. Bertolotti had already asserted that digitate impressions form with great rapidity. Flournoy also reported paralysis of the third nerve, explained by pressure on the nucleus. He also suggests an abnormal inclination of the aqueduct of Sylvius, causing sudden ventricular stasis, as in tumors. If we admit also irregular cerebral growth, not affecting all parts of the brain at once, the irregular and paroxysmal symptoms so often noted in oxycephaly receive an additional explanation.

The intracranial conditions deserve serious consideration, especially in view of the growing belief in the value of operative treatment. Friedenwald's suggestion that increased intracranial pressure was the cause of the blindness, and that it should be treated by decompression operations, remained long unnoticed. There were reasons for this. In many cases of pronounced oxycephaly there was no optic nerve disease; in but few were there papillitis and disturbance of vision. But the evidences of *x*-ray examinations became more and more convincing, and operators gradually attacked the problems. The cases do not seem to me at present to justify an analysis, especially by one not practically familiar with cranial surgery, but some results may be pointed out. Various decompression operations, such as lumbar puncture, trephining, ventricular

puncture, and puncture of the corpus callosum, have been carried out. In many cases there was at least temporary improvement. Deaths following the operation often suggest a comparison with the results of some other kinds of operations in their early days.

Treatment. The first thing to be sure about is the indication for decompression. The symptoms are not always certain, partly on account of the variations, and prolonged observation may be necessary. Skiagrams may not indicate the condition found at the time of operation. In a case of Herzog's it was supposed that intracranial pressure was increased, but at the operation, with puncture of the corpus callosum, no such increase was found. The patient died with meningitis symptoms, but there was no meningitis at autopsy.

The question whether the optic nerve lesions are early or late is important and must be answered as accurately as possible.

Lumbar puncture has the same dangers as in brain tumor. The cerebellum may be prolapsed or sucked into the vertebral canal.

Trephining with ventricular puncture seems the most promising operation. The canal operation of Schloffer seems very severe, and at all events should only be undertaken by one who has practiced it on the cadaver. Operation after blindness has occurred cannot restore vision, but may be useful for the relief of pain or other pressure symptoms.

THE CLINICAL ASPECTS OF CHRONIC MANGANESE POISONING

By David L. Edsall, M.D.,

Jackson Professor of Clinical Medicine, Harvard Medical School,

and

Cecil K. Drinker, M.D.,

Associate Professor of Applied Physiology, Harvard Medical School.

(From the Division of Industrial Hygiene, Harvard Medical School.)

THE comparatively unknown disease caused by long-continued exposure to compounds containing manganese has occurred sporadically since the first description by Couper (1) in 1837. It is an interesting commentary upon national character that the condition was discovered and described by a Frenchman, that his work was amplified in fairly minute detail by six Germans, Embden (2), von Jaksch (3), Seiffer (4), Friedel (5), Seelert (6), and Wagener (7), and that now the florid productive capacity of the United States has furnished a sufficient series of cases to permit a much more assured and thorough description of the entire disease picture.

Couper (1) described five cases, all of which occurred in men employed in grinding manganese dioxide for the manufacture of bleaching powder. The first of Couper's patients came to notice in 1821 and "presented symptoms of paraplegia which, becoming worse, forced him at the end of some months to stop work." After absence from the neighborhood for a year he returned, but never evidenced any real recovery. One year later another workman showed similar symptoms which are described in more detail. There was muscular weakness more marked in the legs than in the arms, so that the patient reeled in walking and leaned forward dangerously when he wished to progress. His voice was low and rather indistinct and he showed marked salivation. General sensations and intelligence were unaffected. It is a tribute to the alertness of Couper that he recognized manganese as the probable cause of

these symptoms, removed this second individual and three subsequent patients from exposure to the dust of the factory, and had the satisfaction of witnessing their entire recovery. In the first case, however, in which the disease had been allowed to progress much further, there was no substantial improvement, permanent disability being the result.

Couper's (1) observations were neglected by writers upon the pharmacology of manganese salts until Kobert (8) in 1883 reviewed the entire subject. His article is designed to set at rest the general questions of the acute toxicity of manganese compounds and the poisonous properties of manganese as compared with other heavy metals. Unfortunately neither Kobert nor any other worker with manganese compounds has made sufficiently protracted experiments to gain information upon the details of chronic poisoning with this metal, and for chronic effects we must look entirely toward the cases that have occurred in man.

Von Jaksch (3) in 1901 described three cases which he believed to be somewhat atypical instances of multiple sclerosis. All three of these individuals worked in the same factory, where they breathed air loaded with manganese dioxide dust. The symptoms they presented are characteristic of manganese poisoning, as von Jaksch (9) himself points out in 1907. Embden (2) in 1901 described four cases which he correctly designated chronic manganese poisoning. He was aware of Couper's (1) observations and gives him credit for being the first to picture this very extraordinary disease. Friedel (5) in 1903 added another case to the last, and Seelert (6) in 1913 made an extended report on the condition of this patient ten years after the first recognition of poisoning. Casamajor (10) in 1913 reported nine cases occurring in a single mill in the United States. These men worked in a dusty atmosphere containing manganese as oxides and silicates. It is noteworthy that all the European cases occurred in manganese dioxide grinders.

It has been our good fortune to examine all the cases seen by Casamajor with two exceptions, and to these we have been able to add examinations of thirty other cases in various stages of the disease. As a consequence we can describe the early symptoms of the condition and its typical course with a greater degree of finality than has been heretofore attained. In this communication we shall

confine our work to such a clinical description, reserving complete details of the condition in its industrial relations for a subsequent article in the *Journal of Industrial Hygiene.*

Etiology. It is of interest to note that in both the European and American cases the disease has followed work in an atmosphere laden with dust containing manganese. In Europe the compound has invariably been manganese dioxide (MnO_2), in this country both oxides and silicates of manganese have been responsible. Although there are numerous instances of acute poisoning from accidental or willful ingestion of manganese compounds, there are no instances of chronic poisoning in which the portal of entry is the gastro-intestinal tract alone. The constant breathing of dusty air results in varying degrees of deposition in the lungs, depending upon the type of dust. In the case of dust containing manganese we have no definite post-mortem information to tell us whether the material accumulates steadily, or whether it is actively removed, so that large deposition is avoided. Several of our cases have reported ability to recognize dust in their sputa two years after leaving the mill. It would seem probable that our patients after several months of work must have provided themselves with a pulmonary reservoir of dust which in part reaches the blood stream through the lungs and in part is coughed up and swallowed. The dust is readily soluble in human gastric juice and the manganese is probably mainly absorbed as chlorides. While certain of the heavy metals, such as lead and mercury, may easily cause poisoning through inhalation, it seems most probable to us that the major part of the absorption in the case of manganese has been from the intestinal tract. It is possible that protracted feeding experiments with dogs, which we now have in progress, will give the answer to the question.

Pathology. Casamajor (11) reports an autopsy on one case, the individual having died of pneumonia some time after stopping work in the dust. The findings are of no importance with the possible exception of a statement that, "There was some degeneration of more or less regular character in the longitudinal fibers in the pons which run with those of the pyramidal tracts. . . . The degenerated portion does not appear to go above the upper level of the pons, nor does the lower portion extend to any appreciable extent into the me-

dulla." Stöcker (12) has called attention to the similarity of the symptoms caused by manganese to those described in detail by Wilson (13) and later by himself as due to progressive lenticular degeneration. We can in many ways confirm this clinical similarity, and later studies may bring out an identity in pathological changes.

Symptomatology. A summary of the history and physical examination of a recent case will illustrate the general character of the disease:

Case. T. B. Age twenty-nine. White. Married. American. June 19, 1918.

Complaint: "Trouble with legs and back."

Family history, past medical history, and habits have no bearing on the present illness.

Marital History. Married February, 1912. First child a girl, born August 29, 1915. Child talks and has been entirely normal in every way since birth. Second child, a boy, born December 31, 1917, entirely normal. Wife has been well and has had no miscarriages. The patient's present illness began in June, 1917, six months before the birth of the second child. No doubt unrecognized symptoms were present before this time, but neither then nor to-day, with the disease at its height, has there been any alteration in the patient's sexual instinct or ability to copulate. (The foreign reports give no evidence of sexual alterations as a result of the disease and there is no evidence of such abnormality in any of the American cases.)

Present Illness and Occupation. A farmer prior to mill employment. Worked first as a laborer in a dusty part of the mill from September 22, 1912, to November 4, 1912. Then, after a short interval in a dust-free job, was assigned as a motor tender in another department from January 27, 1913, to May 2, 1913. This latter work was very dusty, but not so bad as his first task. It, however, caused the development of severe cough with thick expectoration, and this complaint, cough, finally forced the patient to take work in a neighboring paper mill. He remained in the paper mill from May 2, 1913, to November 16, 1915, and re-entered the employ of his old company on the latter date, free from cough and normal in every respect. After varied work in stables, mill yard, garage, and one week in the mill, the patient re-entered very dusty work on May 7, 1917. In both stable and mill yard work the patient was in and out of the mill many times, and was thus subjected through an indeterminate period to dust. It is, therefore, impossible to give the exact length of exposure to dust

prior to onset of first symptoms. During June, 1917, after only one month of steady employment, the patient began to feel "laggy-like," "sleepy," and "weak all over." In July his wife noticed he began to walk "queer" and on August 1, 1917, he was transferred to dust-free work. While so employed, cough, which had begun again, disappeared and the patient believed he would shake off the trouble with his legs. This did not prove true. During September or October, 1917, "cramps" and "stiffness" in the calves became annoying and his legs would "go to teetering" when he sat down. He always noticed that fatigue brought on bad attacks of cramps during the ensuing night and that "teetering" was exaggerated by it. With the onset of cramps and muscular twitching the patient's gait became progressively worse and he was compelled to stop work on November 1, 1917, because of fear of falling. If falling occurred it was straight forward on the knees. He was unaware of retropulsion until examined by his physician on November 1, 1917. There has been no increase in tendency to fall, cramps, nor twitching since leaving work, but on the other hand there has been no improvement. At present he works in his garden during the day, but can only manage short shifts, as he grows tired very easily.

The patient has noticed no mental deterioration—memory for figures, ability to do sums and to write, except for dexterity, is as good as ever. "Gets to laughing and can't stop." No history of similar crying spells nor changes of temper. No abnormal dreams, sleeplessness, visual nor auditory symptoms, nor vertigo. No history of anesthesia, paresthesia, rectal, nor urinary disturbances. No loss of appetite. Moderate constipation while working in the dust.

Physical Examination. Slightly built young man who stands erect without swaying. Ignorant and suspicious type. Laughs inordinately and easily. Memory fair and adheres to statements when made.

Skull: There is a small depressed fracture in the occiput with a large scar beside it, representing birth injuries which have never caused symptoms.

Hair: Normal.

Face: Smooth. Most of the time the mouth is held slightly open and there is a fixed, silly grin which goes over readily into vigorous laughter.

Skin: Good color. No eruptions nor pigmentation.

Eyes: Pupils equal, regular, and react promptly to light and accommodation. No nystagmus and no abnormality in movements of the eyeballs. No restriction of form fields. Fundi not examined.

Nose: No evident obstruction. Is a mouth breather and says he has always snored.

Lips, Teeth and Gums: Normal. No salivation.

Tongue: Protruded in the midline without tremor.

Tonsils and Pharynx: Normal. The patient makes rather frequent large swallowing movements during the history and examination.

Larynx: Speech very slow. Enunciation good, and voice clear but always low.

Thorax, Lungs and Heart: Normal.

Vessels: No arteriosclerosis. Blood pressure not elevated.

Abdomen: Rather rigid. Abdominal reflexes present and hyperactive. No independent twitching in these muscles. No masses nor tenderness in the abdomen.

Extremities—Arms: No wasting nor paralysis. There is a constant coarse tremor of the fingers with the hands outstretched. This is accompanied by frequent periods of twitching, not confined to any one muscle or group of muscles and usually quite rhythmical. Biceps, triceps, and radial periosteal reflexes present, equal and exaggerated. Tremors and twitching not intensified by intention. There is no apparent weakness in hand grip nor in resisted movements of the biceps. Finger to nose and finger to finger tests are made well but rather deliberately, and this slowness of movement characterizes all the patient's activities.

Legs: No paralysis nor wasting. There is almost constant "teetering" in both legs. This means a rhythmical alternation in contractions of the calf muscles and their antagonists. It occurs rapidly and almost ceaselessly during the examination so that the patient's heels are tapping the floor about sixty times a minute. This very gross tremor can be stopped voluntarily, but invariably begins again as soon as the patient's attention is directed toward other matters. Patellar and Achilles reflexes are present, equal, and increased. Ankle and patellar clonus are marked and clonic contractions of all the muscles occur readily on repeated tapping. No Babinski phenomenon. There is no muscle tenderness, and no cramp could be elicited during the examination. When the legs are flexed passively on the thighs there is a steady slight resistance to the movement which the patient does not seem able to avoid. The patient cannot stand in the Romberg position—falls backward. In spite of his own statements to the contrary, he can walk with his eyes shut. In his gait there is marked scissoring and his toe coming forward strikes the opposite heel, tending to trip him. This is what he seems to need to watch and probably accounts for his statement of inability to walk in the dark. He falls at once on attempting to walk backwards. There is no propulsion unless he stands on his toes.

Sensation: Skin, deep sensation, and special senses entirely normal.

Laboratory Examinations. Neither in this case nor in any of those we have examined are there any abnormal findings in the blood or urine. Spinal fluids have, likewise, been negative. Traces of manganese have been found in the urine of workers in the mill in question, but there has been no accompaniment of kidney irritation, and such traces of manganese as occur apparently disappear rather promptly on removal of patient from dusty work.

As we have seen this disease the following positive findings make the syndrome. We have numbered them in the most common order of appearance. It is difficult to emphasize in any written description the clearness with which the symptoms come out and the ease with which the diagnosis can be made.

1. A history of work in manganese dust for at least three months.
2. Languor and sleepiness.
3. Stolid, mask-like facies.
4. Low monotonous voice. "Economical speech."
5. Muscular twitching, varying in degree from a fine tremor of the hands to gross rhythmical movements of the arms, legs, trunk, and head.
6. Cramps in the calves and a complaint of stiffness in the muscles of the legs, the cramps usually coming on at night.
7. Slight increase in tendon reflexes.
8. Ankle and patellar clonus. Frequently by stretching any of the muscles of the body it is possible to elicit rhythmical contractions. Romberg inconstant and no inco-ordination.
9. Retropulsion and propulsion.
10. A peculiar slapping gait. The patient keeps as broad a base as possible, endeavoring involuntarily to avoid propulsion. The shoes are worn evenly, and we have not been able to convince ourselves of the pronounced tendency to walk on the region of the metatarso-phalangeal joints, a feature strongly emphasized by von Jaksch (9).
11. Occasionally uncontrollable laughter, less frequently crying.

Discussion and Prognosis. As one considers such a disease picture a variety of somewhat similar symptom complexes arise in the mind. Von Jaksch (3) believed the first three patients he saw to be atypical cases of multiple sclerosis. The constant absence of nystagmus, eye-ground changes, and intention tremors in the thirty-seven cases we have examined, renders it improbable that the disease

is of this type. In Casamajor's (11) autopsy there was no discovery of disseminated lesions.

In the fixity of expression, the muscular rigidity, the tremors, and in the propulsion and retropulsion there is, of course, a striking suggestion of paralysis agitans. These cases, however, exhibit a striking similarity in their fundamental nature to the disease first thoroughly described by Wilson (13) in 1912 under the title of "Progressive Lenticular Degeneration: a Familiar Nervous Disease Associated with Cirrhosis of the Liver," and since, in this instance, an unusually definite clinical entity is accompanied by equally definite pathological changes, we have felt it of great interest to compare the condition with chronic manganese poisoning. Unfortunately the symptoms of lenticular degeneration are invariably given in greater detail near the death of these patients than in the earlier stages of the disease. Wilson sums up this syndrome as follows (page 478):

> "In pure, uncomplicated, bilateral lesions of the lenticular nucleus, and more generally of the corpus striatum, provided they are of sufficient size and of adequate duration, the clinical symptoms are bilateral involuntary movements, practically always of the tremor variety; weakness, spasticity, or hypertonicity (sometimes spasmodic contractions), and eventually contracture of the skeletal musculature; dysarthria or anarthria and dysphagia, and a degree of emotionalism; but without any sensory disturbance, without any true paralysis, and without any alteration in the cutaneous reflexes. If the abdominal reflexes are absent (apart from muscular rigidity) or the plantars of extensor type, then the syndrome is no longer pure."

The tremors described vary from the finest type to bizarre athetoid movements, just as we have seen them in manganese poisoning. They have further similarities in that they may be inhibited willfully for a short time, but break out again when the patient relaxes his effort at control, and in that the tendency to tremor seems to move about to different parts of the body. Stöcker (12) noted this markedly in his case.

In relation to "the weakness, spasticity, and hypertonicity," sufferers from manganese poisoning exhibit findings very similar to those found in lenticular degeneration. In the latter condition weakness is not pronounced until the terminal emaciation sets

in. We have commented upon the resistance to passive movements noted in manganese poisoning. They show a peculiar, slight hypertonia, active in type, as contrasted with the hypertonia of pyramidal tract disease. This tendency to slight hypertonia seems to us to dominate the entire picture. It results in slow, strained movements, not awkward nor inco-ordinated, but always characterized by over-expenditure of strength. Such efforts seem to account for the economy of words and slowness of speech often so noticeable early in the disease. In this relation we may quote from a private report made by one of us during the past summer, in which the physiological character of the symptoms is discussed:

"If the disease (chronic manganese poisoning) does affect the central nervous system, it seems to do so by cutting off the ordinary inhibitory control upon which we depend for smoothness of muscular action. In normal individuals with contraction of the biceps there is a simultaneous relaxation of the triceps, which allows the biceps to operate easily and without undue load. In the manganese cases the great characteristic of the muscular movements seems to hinge on the absence of just such perfect reciprocal relations. When a patient walks he uses all the muscles of his legs and uses them violently. He gets no return for half of this muscular effort, indeed it resists the movements he wishes to make. The early languor, sleepiness, and fatigue so characteristic of the onset of the disease, arise from the excessive muscular work which the patients involuntarily accomplish in attempting to carry out their mill duties. They are tired out all the time as a result of the over-exertion which every movement entails, and the progress of the disease is often so slow and tedious that they are never conscious of the abnormality of their muscular movements until they fall."

It is significant to find some months after writing this, in Wilson's descriptions of cases of lenticular degeneration, such statements as:

"When the patient was voluntarily contracting, say, the left biceps in the effort to flex at the elbow against resistance, the left triceps did not relax entirely, though it became for the moment less tonic."

And in another case:

"Everywhere the musculature was firm and hypertonic. Of this one could easily convince oneself not merely by palpation, but by impressing passive movements on the various segments of the limbs, when it at once

became obvious that whether the movement were one of extension or of flexion the antagonists were in each case equally resistant to the movement."

Wilson's cases of lenticular degeneration eventually developed true contractures. We have seen but one case of manganese poisoning which suggested the possibility of such development. In our cases removal from harmful environment has prevented such extreme conditions, if indeed it is possible for them to occur.

The low, monotonous speech of manganese poisoning never reaches the condition of anarthria exhibited by cases of lenticular degeneration, nor have we seen, or found described, dysphagia. The "emotionalism" described by Wilson is almost invariably uncontrollable laughter, occasionally weeping; and the manganese cases in certain instances show these tendencies, and they are furthermore identical in the fact that they usually fail to present other mental symptoms.

Wilson mentions marked salivation in several of his lenticular cases. We have not seen this in manganese poisoning, but it is described in two of the foreign cases, Couper (1) and Friedel (5).

Finally, in the entire absence of sensory disturbances the two conditions, lenticular degeneration and chronic manganese poisoning, are strikingly similar. It is significant that in the disease described by Wilson (13) the pathological changes are sharply localized, and in his opinion are due to the action of a toxin which is definitely selective for cells and fibers of the putamen and lenticular nucleus generally. In the case of chronic manganese poisoning it would seem possible that there is the same selective affinity. In the one case autopsied by Casamajor (11) no such lesions are described, and it is very probable that removal from poisonous surroundings invariably causes cessation of the pathological process before very gross damage is done.

Cases of manganese poisoning present a very poor prognosis if far advanced. This has been true in both the foreign and American cases. If tremor and gait disturbances have developed, any considerable degree of recovery is very doubtful, but there is no known shortening of life. The patients are hopeless and long-lived cripples, since manganese brings about none of the life-shortening degenerations common in some other metallic poisons.

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A SIMULTANEOUS GASTRO-DUODENAL ASPIRATOR[1]

By Max Einhorn, M.D.,

Professor of Medicine at the New York Postgraduate Medical School, New York

FRACTIONAL examination of the gastric contents is nowadays frequently done by clinicians, the duodenal tube having made this innovation possible. The duodenal contents can, likewise, be examined by the fractional method. The study of the curve of the alkalinity of the duodenal contents is probably of greater import than that of the gastric acidity.

Whenever an examination (fractional) of both the gastric acidity and of the alkalinity of the duodenal contents is desirable, the

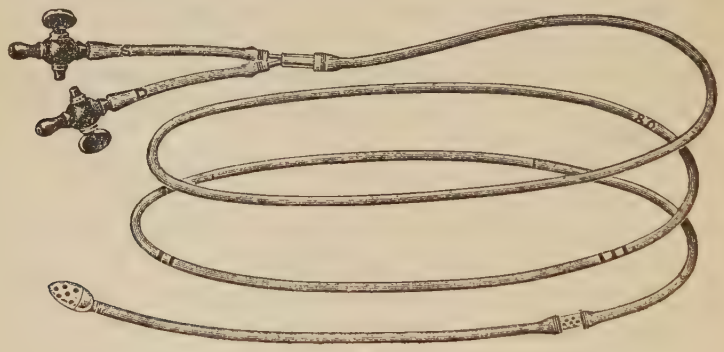

Fig. 1. The Simultaneous Gastro-duodenal Aspirator.

S, branch running to stomach; *D*, branch running to duodenum.

patient up to now had to be subjected to two different test meals on two days. In order to facilitate this examination for the patient and also to increase its worth I constructed a "Simultaneous Gastro-duodenal Aspirator." By means of this instrument gastric and duodenal contents can be obtained at the same time, and comparisons made between the workings of these two divisions (stomach and duodenum) of the digestive apparatus.

The gastro-duodenal aspirator (see Fig. 1) consists of a long

[1] Demonstrated at the Clinical Society of the Lenox Hill Hospital on October 11, 1918.

soft rubber tube (about 12 F.) with two separate canals, one leading to a perforated end capsule, the other to a perforated hollow metal piece, lying about 25 cm. above the end capsule (or proximal end of the tube). The distal end of the tube branches off into two side tubes provided with stopcocks (marked *D*, duodenum, and *S*, stomach). Like the simple duodenal tube, the gastro-duodenal aspirator is provided with the usual markings, starting from the capsule end.

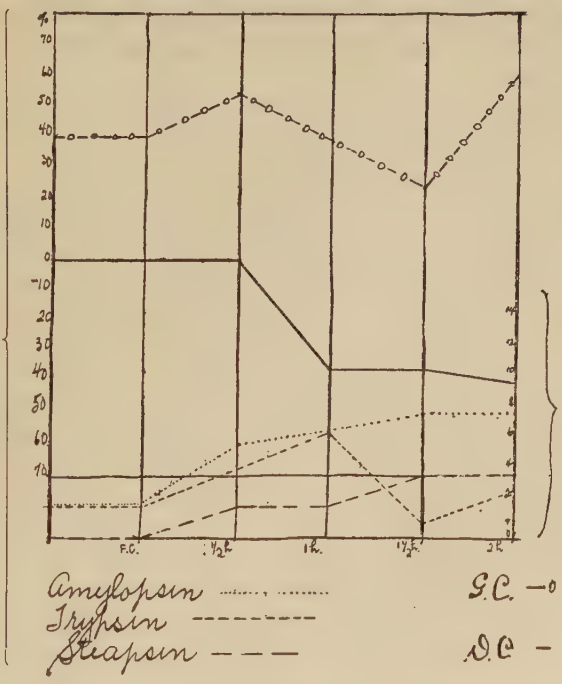
Reaction Curve of Acidity and Alkalinity Expressed in Number of c.c. of 1/10 Normal NaOH or HCl Solutions Respectively, Enough to Neutralize 100 c.c.
Activity of Ferments Expressed in mm. of Agar Tubes Digested.
F.C.
½ h.
1 h.
1¼ h.
2 h.
Amylopsin
Trypsin
Steapsin
S.C. –o
D.C. –

FIG. 2. SIMULTANEOUS EXAMINATIONS OF GASTRIC AND DUODENAL CONTENTS IN FASTING CONDITION AND AFTER BOUILLON.

Mark I is situated at 40, mark II at 55, mark III at 70 cm. from the capsule, and ultimately 80 cm. is stamped on the tube.

When the aspirator is in the digestive tract and the capsule has reached the duodenum, the perforated metal piece is within the stomach, provided the capsule is at a distance of 60 to 78 cm. from the lips. All along this position of the aspirator it will be possible to obtain gastric juice and duodenal secretions simultaneously.

Mode of Procedure. The gastro-duodenal aspirator is introduced in the same manner as the usual duodenal tube. When the instrument

has reached the duodenum it is best to first let it slip down to the 80 mark. The tube is then pulled out a little bit from the mouth, so that about 2 cm. in front of the 80 mark are outside of the lips. At this moment aspiration of both stomach and duodenum can be performed. Fractional examinations of the stomach and duodenum can also be undertaken at the same time.

The curves in Fig. 2 of the acid secretion of the stomach and the alkalinity of the duodenal contents, observed on the same patient at the same time, illustrate the practicability of the gastro-duodenal aspirator.

THE NATIONAL ORGANISATION OF MEDICAL RESEARCH IN PEACE AFTER WAR

By Sir Walter M. Fletcher, K.B.E., M.D., Sc.D., F.R.S.
Fellow of Trinity College, Cambridge, and Secretary of the British Medical Research Committee

WITHIN a fortnight of the Armistice I had the happiness of meeting the members of the American Red Cross Medical Research Committee in Paris—a Paris gay with bunting and bright with new light, freed from the long tension of doubt and anxiety and not yet plunged into the cares that attend the new birth of Europe. Magical sunshine lit the frosted Tuileries gardens in the cold mornings; bright moonlight flooded them by night, shedding its austere benediction on the brilliance of the serried lights that sparkled along the city and the bridges, of the lights shining in the Place de la Concorde above the disconsolate German guns, and of the answering lights below, returned from the dark and flowing spaces of the Seine.

This was the setting of place and occasion in which those last meetings were held, and it is not to be wondered at if they were charged with some air of emotion from the past and a keen sense of possibilities within the future. Feelings of this kind made a background for the sober scientific discussions held in conference, while in the Research Committee room itself there was, I think, behind the normal flow of business, an unconfessed but lively apprehension at once of the now obvious brevity of past opportunity and of the uncharted prospects seen in the years approaching. Those days were full of significance and interest. I was meeting many friends, as well as others already long and well known except in person, and of all these many had already given their wholehearted collaboration and sympathy to the British Medical Research Committee in their work for the medical services in the field and at home. It was natural that much should come to be said at such a time of the methods of planning research work, not

only in war conditions, but in peace. The possibilities of there being maintained in permanent form hereafter organisations like those of the National Research Council at Washington with all its branch activities, and of the Red Cross Research Committee itself, were explained to us; we, on our part, were asked for the ideas being formed upon the British side in the direction of State aids for scientific work. From many sides expression was given to the growing hopes that in the future of peace there might be preserved and strengthened all those common ties between American and British science that we had come already to value so highly.

Discussions of this kind, and so begun, are likely to be long lived and to become endemic. Some of the considerations that have offered themselves I should wish, however unworthily, to set out here, in affectionate homage to Sir William Osler, that "greatest common factor" of British and American Medicine, whose life has been given for the progress of medicine in both countries alike and for the interchange of all that is best in the medical fields of either of them.

To speak of the "organisation" of research at all is to use a contradiction in terms, if we have in view that highest type of research by which knowledge of new kind is gained, and new roads are opened for the workers who follow. We might speak as fitly of the "organisation" of poetic achievement or of musical composition. Those who can work fruitfully at the growing points of knowledge, who can make gains upon the ocean of the unknown, are poets indeed, using the highest gifts of poetic imagination, on their way to building by laboured observations the fabric they have already guessed or dreamed. No agency can "organise" or prepare for the romantic vision of a Newton or a Faraday, a Darwin or a Pasteur, or even for that of lesser leaders. But public and private action can aid men of this kind by setting them free from hindrances in their work, by teaching the world to give thanks for their gifts and to pay them due honour. What Queen Mary, all unknowing and a century beforehand, did through her endowment of Trinity College for Newton we know, and we know what the Royal Institution did for Davy, and for Faraday, and what the private accidents of family fortune did for Darwin. Yet without those material supports all these might have passed unknown, as no doubt full many a

"mute inglorious" poet of science has passed already, to our immeasurable loss.

Yet in the new regions revealed by seers of this kind there are fields to be surveyed and divided and tilled, new roads and communications to be established. For this secondary work the labourers have to be found, to be set free from other cares for the task, and though they may press like hounds on the leash to follow the tracks of their leaders, great gain may come, if only through economy of effort, from a co-ordinated direction and mutual assistance. So much, no doubt, is beyond dispute, but a question to be faced and answered is whether this material assistance and centralised guidance are to be given by the State as such, or left to the chances of accident and of private good will. In so far as staff-work is needed for the army of workers following the pioneers of science, or, to change the metaphor, in so far as deliberately arranged gang-work is needed for labourers engaged in completing the design of the architect, is this central agency of direction to be offered, and are wages to be paid, by the State, and more properly and usefully by the State than otherwise?

If regard be paid to the immensity and difficulty of the work, to its spiritual and intellectual interest no less than to its material and economic value, no clear-sighted community would leave its advancement to chance and to the voluntary efforts of workers whom chance has set free; nor would they leave it to sporadic private beneficence—at least not until a Utopia had been reached in which private beneficence had become wholly sufficient. Yet it may be, and in England has often been, argued that the State endowment of research is less desirable than its private endowment, and that organisation effected by State action is actually harmful or, at the least, fraught with danger to the freedom and the best development of enquiry. This fear of what is sometimes called "State control" has probably spread from the sphere of education, in which, whether reasonably or not, it had earlier shown itself, to the neighbouring field of research. Sir William Osler has himself had occasion to dispel some *laissez faire* alarms of this kind. He wrote in 1914:

"Is freedom of research necessarily shackled in Government harness? Certainly not in autocratic Germany, where the Reichsgesundheitsamt

was the centre of the free and brilliant researches of Koch and his colleagues, not only missionary researches in many parts of the world, but practical health campaigns, such as that against typhoid fever, which could never have been undertaken without strong official backing. Certainly not in democratic America, in whose Government bureaus Theobald Smith initiated those epoch-making studies on protozoal disease, in which Walter Reed and his colleagues solved the problem of yellow fever, and from which Stiles started a world-wide campaign against anchylostomiasis—all memorable and life-saving investigations. The studies of Anderson on typhus, of Rosenau and his associates on anaphylaxia, and the new chapter in plant pathology opened by Erwin Smith are additional tributes to the freedom of research under Government control."

All depends here upon the content of the word "State." If by the State is meant in a democracy the Government of the day acting through administrative officials, then if the State attempted to organise or direct or control research, the results would undoubtedly be harmful, so far as any results would be obtained at all. This possibility need not perhaps be considered seriously, and indeed already other and obvious lines have been laid down for the organised endowment of research so far as the British Government has already undertaken to maintain it. Already in three main directions the Government has assigned large sums for the State support of research work and has designed apparatus for their application in aiding and co-ordinating enquiry. Apart from small, almost negligible, aid given earlier to research through various executive Government Departments, or through the Royal Society, the first important special provision was made in 1909 for the assistance of research in agricultural science by the so-called Development Commission. In 1913 the Medical Research Fund was established and put under the administration of the Medical Research Committee. In 1915 when the war had suddenly brought home to the legislature our neglected national opportunities, much larger sums were made available for Scientific and Industrial Research under the control, in practical effect, of an Advisory Council attached to the Privy Council. In each of these three instances the operative regulations were so framed as to put the available funds at the disposal of a small group of scientific men appointed for the purpose, and in general it may be said that a progressive advance has

been made towards securing, by regulation, that these men shall represent the best available counsel of the scientific community at a given time in the particular fields of their work.

It is true that in a democracy the representative Parliament must be at all times absolute, and that scientific councils or committees charged with the administration of State endowments for research can derive power only through a Minister responsible to Parliament, and so must be accountable to him. For those who think a democracy is to be feared rather than to be educated, nervousness here has its place. Parliament could in theory, and might in practice, interfere disastrously with the scientific councils engaged in maintaining and organising scientific work by State money given for the purpose. But so equally Parliament could interfere, and has not seldom been suspected of interfering, with the work of Generals in the field of battle, though the risks of lay interference with experts is actually greatly less under a democracy than under an autocracy.

Subject to this necessary minimum of responsibility to Parliament, full effective control of the detailed expenditure of the research funds for the advancement of knowledge must be left, and in practice is left, in the hands of scientific men. The British Medical Research Committee, already mentioned, was constituted in 1913 upon that principle. It is a Committee of nine, containing six scientific men, who, though they are chosen not as representing either particular interests or institutions, but rather for their personal qualities as good counsellors, are taken from different branches of the medical sciences. With these are three lay members, chosen from members of Parliament—one (as it happens) from the Lords and two from the Commons. Of these nine members three normally retire every two years. The lay element, in a minority, is valuable to the work of the Committee, for it brings financial and administrative views from outside to aid the balance and direction of the technical work of the scientific advisors. It is to be noticed, above all, that this Committee have no administrative officials or machinery standing between them and the Minister. They address him directly, and within the widest limits are left free to shape their policy. In their financial arrangements, though subject of course to strict audit, they have every reasonable liberty

to make the best disposal of their means to secure their scientific ends.

This absence of administrative machinery above the heads of the Committee and the absence of executive lay officials between them and the Minister is a matter of vital importance. There is no executive officer in power to urge them towards quick results and rapid discoveries, none to delay proposed researches as academic or apparently aimless, or to postpone the announcement of scientific results that might seem to throw inconvenient light upon established practices. The essence of research is dissatisfaction with the known. Its business is to open new windows for the light, and open windows may often bring draughts to those settled in old habits within. The intellectual freedom of this Committee and of its companion research Councils is the first condition for the vitality of their work.

It will be seen that this method of linkage between the scientific activities of the country and the State does not submit science to State control, but is rather the organising of science itself. It uses a democratic principle of representation for the proper distribution of what the State offers to research, and for the proper conveyance of the knowledge gained by scientific work towards the guidance of State activities.

It will be seen also that any one of the National Research Councils already noticed, of which the Medical Research Committee may be taken as the present example, must have functions of two chief kinds. It is first the conduit through which State resources for research are to flow, and it will therefore make research grants for the endowment of enquiry in all the parts of its proper scientific sphere, using as the *locus* of its work the universities and other scientific institutes, supplementing these, if need be, whether permanently or temporarily, by the establishment of a special centre of work immediately under its general direction. In the second place the Council or Committee must have intellectual responsibility. It must dispense State assistance with a clear eye to the intellectual objects to be secured; it must not distribute doles to workers upon simple demand or spread grants with any artificial uniformity in geographical distribution. Its members must take for the time being the responsibilities of a directing staff; they must

judge relative values; upon occasion they must decide priorities. They must gauge as best they can the directions in which work can be done with the best economy of time and effort. They must pay regard to what is already being done elsewhere and act so as to help it, if need be, by supplement. They should be able to bring workers geographically separate into intellectual union, and so gain the advantages of team work among men who may be in laboratories far apart. All these are high and difficult tasks, and no Committee will dare to look for more than partial success. The effort would be idle altogether unless the Committee acted as the representatives for the time being of the scientific workers themselves, as indeed they are, and acted, moreover, in close co-operation with them. In practice, however, these conditions have been found easy to secure, and they have been gained in the main by using freely the well-tried method of forming groups of workers into sub-committees or commissions for particular lines of investigation, and to groups of this kind many of the formal powers of initiation and even of finance, resident in the National Committee, may be delegated to any given degree.

It is in Medical Science above all that the device of gaining direction of research work by conference of workers, and by the adoption of "team work" to fit the differentiation of powers and functions among the workers is most patently useful, and even necessary. The branches of natural science can be truly classified after all only in terms of their technical methods and particular laboratory needs. The chemist must be separated, for instance, from the experimental physiologist, not by any difference of intellectual method, but only because their tools and their workshops are different. In medicine there is no branch of science and no kind of technical method which may not have to be laid under contribution. The study of an infection will involve bacteriological work upon the parasite, the physiological studies of reactions in the body, the chemistry of the conditions of bacterial growth, and of its results, and of the interplay of these in the body fluids; further, it must introduce the physicist to give meaning to the stock phrases of "agglutination," "opsonins" and the like, and these diverse enquiries must have added to them the observations of the physician and the descriptions of the morbid anatomist. Medical science has

suffered perhaps more than any other compound science from the inevitable separation of sister studies on account of their diversity in working equipment and *habitat*. Investigators along fruitful lines are continually baulked by some obstacle not surmountable except by a return for long training in other methods of work. No man can play all musical instruments with skill, and in science no man can have at command all technical resources of investigation. The complexity of many medical problems demands, so to speak, an orchestral performance, and success can be attained only where each contributor is using high skill in his chosen and cultivated art, bringing into play all his acquired knowledge and experience, and when the products of all these are combined in harmony together.

Organisation in this sense we have always had, but it has been sporadic only and incomplete. If the minor dangers of State organisation are well removed by basing it upon the consenting help of all the workers, it will allow the centralised direction not only to bring effectively into play the financial resources of the State, but also to make abundant and effective the co-ordinated work of the whole army of investigators. These benefits the State can bring to research, and it should be noted further that this relation between Government and science brings a reflected benefit of immense potential value to the power of Government itself. It is a commonplace to say that research work of the highest intellectual interest and scientific value may spring from enquiries directed at first only to a practical need of the moment. No true enquirer can be purely utilitarian; the poetic curiosity of the scientific man, upon which all growth of knowledge depends, pays no heed to utility. It is no less a commonplace, however, to point to the material boons which researchers leave behind them in their wake, perhaps most commonly for others to gather and apply. A centralised agency for linking the State with the laboratories of science may form from time to time an invaluable clearing house by which even the disregarded by-products of work arising from the problems of one executive department of Government may be turned to the immediate benefit of another. Of this the history of the war has provided innumerable instances.

We are not to be concerned here with details of the work actually done by the British research organisations during the war. The

success of organised enquiries, here as well as in and for the United States during their shorter period of war, are well known, or are to be found easily upon record. The war has been won by the bravery and endurance of sailors and soldiers, merchant seamen and industrial workers, but the tasks of all these would have been infinitely more difficult, and their valour and virtues must in the end have come to naught, save for that "heeded prayer" of "active brain" and for the work of scientific men, done for the most part invisibly. New knowledge has been necessary in countless ways, and old knowledge has been needed in fresh combinations; these have been made effective within the short allotted time only through organisation and common effort. We might well take as a motto for the modern process of war that ancient meditation of Bishop Hall of Norwich, who sprang, like John Harvard, from Emmanuel College, Cambridge:

> "There never was good thing easily come by. God sells Knowledge for Sweat: and so he doth Honour, for Jeopardie."

We desire new knowledge for our minds and need it for our affairs, not less, but even more now that peace approaches, and nowhere is this seen more clearly than in the sphere of medicine. Here indeed there can be no peace, for "the last enemy that shall be destroyed is death." If for this lesson there needed fresh teaching it has surely been given to us in pain enough already; for in the few months that have passed since the war was virtually ended the scourge of influenza has already taken more lives than those of all the men killed during four years of the greatest carnage of battle the world has ever seen.

For a national system of endowment and organisation of medical research, finally, a new argument and justification may still come to be supplied. The needs of war brought at once a centralised and Federal organisation at Washington in the National Research Council, and this had a distinctive medical division. While this was active at home the Red Cross Research Committee was engaged in parallel work at the seat of war in France. If this national apparatus for enquiry in war be maintained upon a peace footing, as so many have hoped, we have at once not only two allied Government systems aiding medical research, but also new possibilities of

liaison between the corps of research workers in the two nations, and we shall have opportunities for international co-operation of a new kind. Relations between scientific men and scientific societies divided by the Atlantic have long been cordial and fruitful, but to these might be added fresh bonds between the national research councils on either side. Here again it is medicine, gathering up into itself as it must the activities of so many technical divisions of science, that has specially to gain by co-operative effort. It is possible, indeed, to look beyond the exchange of ideas and the sharing of work in surveys and investigation, that links between the national councils might bring, and to see in the centralisation by Government endowment, co-ordinated perhaps with the private endowments that are so much more prominent in the United States than in Britain, new mechanisms for the interchange of visits by young research workers of the two nations. So we might hope to see in the perennial quest for knowledge and the long combat against disease some, at least, of our battalions brigaded again together, as of late they marched and fought in battles of another kind to gain the only liberty and peace in which truth could grow or life seem worth preserving.

INTRASPINAL THERAPY IN NEUROSYPHILIS

By John A. Fordyce, M.D., New York

MODERN diagnostic methods and modern treatment, controlled by the Wassermann reaction in the blood and spinal fluid, together with other standardized spinal fluid tests, have made the study and treatment of syphilis the most absorbing and fascinating subject in medicine. Exact knowledge has largely replaced vague clinical impressions, so that we are able to prognosticate the future of a patient affected with the disease with more certainty than in any of the other chronic infections. New facts are being slowly acquired as to the behavior of the spirochætæ when they enter the blood and lymph streams, their sites of predilection, and the tissue responses which they call forth. Many of the older views as to the late implication of the nervous system, the cardio-vascular apparatus, and the viscera are in many respects erroneous, as they are based entirely on the end results of the infection and disregard the pathological processes during the long period of so-called latency. Knowledge acquired by clinical study, serology, and autopsy findings leads to the belief that foci are established in the various tissues which may require years to modify or destroy functional capacity.

The majority of patients with syphilis receive treatment with more or less regularity and intensity. A complete cure is the exception rather than the rule unless treatment is begun in the early months of the infection. The progress of the disease is delayed or held in check for months or years, but is frequently subject to relapses and slowly progressive tissue degenerations. An aortitis or aortic insufficiency is not the result of a sudden invasion of the aortic walls or valves by spirochætæ many years after the primary sore, but the effect of a slow tissue reaction due to the implantation of the organisms in the florid stage of the disease, manifested first by a lymphocytic and plasma cell infiltration about the small vessels of the adventitia and media followed by a replace-

ment fibrosis and disturbance of function. When, therefore, an aortitis is diagnosed it has probably been in existence for years, and finally reveals itself by gross clinical signs attended by more or less functional impairment.

The pathological studies of Warthin in visceral syphilis, which show that spirochætæ may be harbored for years with slight or no reactive phenomena, support the theory of the persistence of the infectious agent *in loco*. Additional arguments in favor of this hypothesis are also afforded by the reappearance of late lesions in the skin or mucous membranes at or near the site of early ones, and the recurrence of keratitis in congenital lues. It is easy to suppose that the spirochætæ behave much the same way in all the organs they invade. We may, therefore, transfer our argument to the central nervous system. With its more specialized centers and tracts spirochætal attacks may cause marked subjective or objective symptoms and signs like headache, delirium, or paralyses of the most varied types. On the other hand, an individual so infected may remain free from all symptoms for years, until some important center or tract is compromised. The patient is then said to have developed neurosyphilis five, ten, or twenty years after the primary infection.

If we admit that neurosyphilis, like its prototype in other organs, may have long periods of latency, it is not difficult to believe that the spirochætæ gained entrance to the nervous system in the period of their greatest dissemination, i.e., the florid stage. Since attention has been directed to early neurosyphilis, careful clinical examination has uncovered a much larger number of cases. More definite knowledge has been acquired by spinal fluid examination at this time. It has been shown by numerous observers that from 25 per cent to 35 per cent of patients in the first year of the infection show pathological changes in the spinal fluid. In some of these patients, after minor damage to the meninges, tracts, or cells, the infection may spontaneously disappear or be cured by treatment. This statement is confirmed by the observation of cases of abortive tabes with pupillary changes and slightly altered or absent deep reflexes, with negative blood and spinal fluid findings. In our routine examinations of neurosyphilitics we have records of a number who have remained stationary for years, and have

presented a negative serology after repeated investigations. The more usual course is the establishment of foci in the cerebrospinal axis which progress with varying degrees of rapidity and eventually lead to one or the other well-known types of neurosyphilis.

To make my position clear regarding the indications for intraspinal therapy, I desire to emphasize the statement that the method is of value in certain types of neurosyphilis which fail to respond to treatment by other channels and in which the spinal fluid reveals an active syphilitic lesion. If a patient, after intensive treatment with arsphenamine, mercury, and potassium iodide, shows little or no improvement in his symptoms, blood, or fluid reactions, some other method of therapeutic attack would clearly be indicated. Rapid and decided clinical and serological improvement following the introduction of a new factor, even though the original procedure might be continued, would strongly suggest that the new factor was responsible for the change. The preparation of a proper serum necessitates a preliminary intravenous injection, so that it would be difficult or impossible to comply with the criterion established by our critics and use the intraspinal therapy uncomplicated with other procedures. Intensive intravenous arsphenamine injections are not infrequently followed by jaundice, dermatitis, or other symptoms of arsenic poisoning, making it necessary for these patients to receive their serum from another treated case.

Invasion of the central nervous system occurs during the acute secondary stage of syphilis, and often manifests itself in spite of intensive treatment with arsphenamine and mercury, as exemplified in Case I. This early meningitis or meningo-encephalitis continues to progress until the new factor intraspinal therapy is introduced. It then declines with great rapidity. Will our unprejudiced critics accept such evidence? The arguments employed against salvarsanized serum in neurosyphilis would apply with equal force to the use of antimeningitis serum in cerebrospinal meningitis. The latter serum is effective, however, only when introduced into the spinal canal.

I have demonstrated again and again in my laboratory the persistence of positive phases in the spinal fluid in patients treated in the most intensive manner by the orthodox methods over long periods, with little or no change except in the cell count and slight

clinical improvement. Intraspinal therapy has been followed by persistent negative phases and clinical improvement or cure. I am, therefore, becoming more and more convinced of its value, and believe the failure of others to obtain like results to be largely dependent on imperfect technic and early discouragement because of slow results.

Since adding salvarsanized serum to 30 or 40 c.c. of withdrawn fluid and permitting the mixture to return slowly by gravity, the results have been more rapid and striking. In this manner a larger quantity of spinal fluid is medicated and possibly a positive pressure established. In seventy-five cases of various types of neurosyphilis all the findings are negative, many of them persistently so for periods of one to three years.

The introduction of salvarsanized serum into the spinal fluid of a patient with a lesion of the posterior roots is often followed in the early period of treatment by severe root pains. After the second injection the reaction is less severe and finally disappears. At times some of the phases in the fluid become more intense, such as increase in the globulin and rise in the cell count. The tabetic pains and other symptoms existing before the injections, disappear or are markedly modified, and generally in proportion to the intensity of the reaction. Similar reactions have appeared after intravenous treatment, but are usually less pronounced and followed by less improvement in the lightning pains. They have also been noted in cerebrospinal meningitis and in focal brain lesions.

Syphilitic patients in every stage, from the appearance of the primary sore to the development of well-marked tabes or paresis, come under my observation. As a systematic examination of all these cases is made, including the spinal fluid, a larger percentage of patients in the preparetic or pretabetic stage is seen. Careful neurological examination may show pupillary changes or alteration in the reflexes or other evidence of involvement of the neuro-axis, but some are without somatic signs. A larger number are met with showing serological evidence of syphilis in the absence of objective signs than patients with positive signs of syphilis showing negative fluid reactions. Because of the character of my work, these cases are detected earlier than those which consult the neurologist and are for that reason more amenable to treatment.

A proper grasp of the treatment of neurosyphilis in its multiform manifestations can be acquired only by a prolonged study of the serology of the spinal fluid as correlated with the clinical symptoms. Indications for and the control of treatment are more accurately afforded by the findings in the fluid than by any other method at our command. The activity of spirochætæ in the central nervous system is reflected, with rare exceptions, in the fluid, so that we are able to obtain with a fair degree of accuracy indications which favor or oppose this treatment, due regard being had for the clinical signs or symptoms. The serology of the more usual types of neurosyphilis is shown in the accompanying table, based on a study of 5000 spinal fluids.

CORRELATION OF SEROLOGY WITH CLINICAL NEUROSYPHILIS FROM AN EXAMINATION OF 5000 CEREBROSPINAL FLUIDS

	Cerebro spinal Fluid				
	Serum	Cells per cmm.	Glob.	Wassermann	Gold Sol.
Tabes.					
a. Progressive.	Positive in 70 per cent.	30–350 or more.	Strongly positive.	Positive in high dilutions.	Luetic curve.
b. Stationary.		0–25	Positive or negative.	Negative or positive in low dilutions.	Negative or luetic curve.
Paresis.	Positive in 98 per cent to 99 per cent.	25–350 or more.	Strongly positive.	Strongly positive in high dilutions.	Paretic curve.
Cerebrospinal Syphilis.					
Meningitis.	Usually positive.	As high as 2000 or more.	Strongly positive.	Usually positive in high dilutions.	Luetic or paretic curve rapidly changed to luetic curve by treatment.
Meningo-encephalitis. Meningo-myelitis.	Usually positive.	Slight or great excess.	Usually strongly positive.	Usually positive in high dilutions.	Luetic or paretic curve rapidly changed to luetic curve by treatment.
Arteritis or endarteritis.	Positive or negative.	No increase.	Positive or negative.	Usually negative.	Negative or luetic curve.
Meningo-arteritis.	Positive or negative.	Usually excess.	Positive or negative.	Positive or negative.	Negative or luetic curve.
Gumma.	Positive or negative.	None or excess.	Positive or negative.	Negative or positive in low dilutions.	Luetic curve or negative.

A pure type of arterial syphilis of the brain or cord with a negative serology, or with only an excess of globulin and a low cell count,

affords no indications for intraspinal therapy. In this condition dependence must be placed solely on antisyphilitic drugs given by the usual channels. The advocates of the intraspinal method have always insisted on the presence of definite serological and clinical indications for its employment, and have favored, in the majority of cases, the preliminary use of drugs in the ordinary way. In rapidly developing optic atrophy, or in other cases where long experience has shown the futility of intravenous therapy, the method should not be too long delayed. Many of the patients who consult me for neurosyphilis have been treated intensively by all the available methods without affecting the clinical symptoms or the serology. In such patients it would be a waste of time to repeat a procedure which has failed.

An early syphilitic meningitis with a high cell count with other positive phases offers the most favorable prognosis. The sooner the meningitis is detected and treated the more rapid the response to treatment and the less the danger of involving the underlying brain tissue. As these cases may develop during active treatment with salvarsan intravenously combined with mercury and progress in spite of such treatment, further use of the methods in question is insufficient and is apt to be followed by disaster.

The accompanying chart shows the rapid results which followed intraspinal therapy.

Case I. *Syphilitic Meningitis.* L. Physician, æt. thirty-two. Initial lesion of thumb in November, 1916, followed by secondaries. Treatment begun with appearance of latter. Two months later right-sided parietal headaches. Lumbar puncture made in May, 1917, was said to show 104 cells with the other findings weakly positive. After seventeen injections of arsphenamine his headaches did not entirely disappear and became more intense a few months later. He suffered from insomnia, great depression, and impairment of mental processes. He lost 24 pounds in weight. Was first seen November 20, 1917, when he complained of severe headache, nervousness, and insomnia. On November 26 he became very excitable and developed a delirium lasting several days.

Treatment from November 23, 1917, to February 9, 1918: Eight intravenous injections salvarsan; 7 intraspinal injections salvarsanized serum (Swift-Ellis, fortified with $\frac{1}{6}$ to $\frac{1}{4}$ mg.).

Results: After three intravenous and two intraspinal injections patient's mental condition entirely cleared and his headaches disappeared. A report

received from him recently states that he feels unusually well mentally and physically and is able to look after a large practice without inconvenience. He has no insomnia and has returned to normal weight.

Cerebrospinal Fluid

Date	Cells	Globulin	Wassermann	Gold Sol	Serum
11–28–17	416	3+	4+ 0·4 c. c.	1123321000	11–28–17 –
12– 8–17	43	+	4+ 0·6 c. c.	1123221000	2– 9–18 –
12–22–17	11	+	3+ 0·8 c. c.		3–25–19 –
1– 5–18	7	±	4+ 1·5 c. c.		
1–19–18	2	±	– 2·0 c. c.	0000000000	
1–30–18	0	±	– 2·0 c. c.		
2– 9–18	1	–	– 2·0 c. c.	0000000000	
3–25–19	2	–	– 2·0 c. c.	0000000000	

I see from time to time patients shortly after the secondary stage who give histories of obstinate headaches, vague phobias, depression, irritability, loss of memory, and other obscure mental symptoms. These patients have received active treatment since the early stage of their infection. They have been thoroughly dosed with mercury and salvarsan with little impression on their symptoms or Wassermann reaction. They usually show some alteration in their pupillary reactions and deep reflexes. The spinal fluid may reveal a high cell count with strong globulin and Wassermann reactions. A paretic gold sol curve may also be present, as in the following:

Case II. *Pre-Paresis.* (?) D., æt. thirty-six. Chancre of index finger and secondaries in February, 1913. Treatment: 12 injections of salvarsan, 46 injections mercury salicylate, 25 injections gray oil, several months of mixed treatment. His Wassermann was negative on several occasions, but with cessation of treatment became positive again. Patient was very apprehensive and nervous most of the time. He passed from observation for a year and when seen in May, 1916, was nervous and excitable; his pupils were irregular, slightly unequal, but reacted promptly to light and accommodation. All the deep reflexes were hyperactive, the left more so than the right.

Treatment from June 8, 1916, to February 12, 1919: Four intravenous injections salvarsan. This treatment had to be discontinued owing to severe reactions; 33 intraspinal injections (Swift-Ellis, fortified with $\frac{1}{10}$ to $\frac{8}{10}$ mg.); 12 injections of mercury; several courses of potassium iodide and mixed treatment.

Results: Patient feels perfectly well, is free from nervousness and excitability and does his work without effort.

Cerebrospinal Fluid

Date	Cells	Globulin	Wassermann	Gold Sol	Serum
6– 3–16	172	3+	4+ 0·2 c. c.	5555430000	2–20–13++++
6–24–16	116	4+	4+ 0·2 c. c.		6– 2–13 –
7–21–16	45	3+	4+ 0·4 c. c.		2–21–14 ++
8–26–16	10	3+	4+ 0·4 c. c.	5555420000	11–20–14 –
10– 7–16	8	2+	4+ 0·6 c. c.		2–24–15 ++
11–18–16	12	2+	4+ 0·6 c. c.	5554420000	6–19–15 –
12– 9–16	9	2+	4+ 0·6 c. c.		9–29–15 ++
1– 6–17	10	2+	4+ 0·6 c. c.		12–15–15 –
2–10–17	7	2+	4+ 0·6 c. c.	5555432000	5–20–16 +++
3–31–17	9	2+	4+ 0·6 c. c.		8–26–16 –
4–28–17	6	2+	3+ 0·6 c. c.		10–28–16 –
6– 9–17	0	+	3+ 0·8 c. c.	5555442100	11–18–16 –
7– 7–17	5	+	4+ 1·0 c. c.		4–28–17 –
8– 3–17	3	±	2+ 1·0 c. c.		1–12–18 –
10– 6–17	3	±	4+ 1·5 c. c.	5555421000	7–27–18 –
11–24–17	2	±	3+ 1·5 c. c.		2–12–19 –
12–22–17	1	±	4+ 1·5 c. c.		
1–12–18	6	±	4+ 1·5 c. c.		
2– 2–18	2	±	4+ 1·5 c. c.		
3–23–18	2	±	4+ 1·5 c. c.	5554421000	
4–13–18	4	±	2+ 1·5 c. c.		
5– 4–18	1	±	3+ 1·5 c. c.		
6–15–18	1	±	3+ 1·5 c. c.	4455431000	
7–27–18	3	±	4+ 1·5 c. c.		
9–11–18	2	±	4+ 2·0 c. c.	2223100000	
11– 9–18	2	±	4+ 2·0 c. c.		
12– 7–18	2	±	4+ 2·0 c. c.	1223100000	
1–11–19	3	±	4+ 2·0 c. c.		
2–12–19	1	trace	– 2·0 c. c.	1233210000	

In these cases response to treatment is slow, and only after prolonged use of intraspinal injections do we obtain modified reactions. The symptoms abate or disappear only to return when treatment is discontinued. The slow therapeutic response is in marked contrast to the earlier types of meningitis, and indicates a probable implantation of spirochætæ in the brain itself and their relative inaccessibility to the drugs. These cases are, in my opinion, potential paresis, and probably are delayed in their progress by the prolonged treatment. In some of them the process is apparently permanently arrested, as in this case:

Case III. *Pre-Paresis.* (?) A., æt. forty-two. Infection in 1905; treatment for seven years with mercury internally and by injection. In June,

1915, he had a convulsion and was unconscious for one-half hour. The attack was attributed to colitis and intestinal absorption, and treatment directed against this until December, 1915, when he had a second convulsion. At this time he came under observation complaining of physical exhaustion and loss of interest. His mental condition was hazy, he showed memory defects, and was markedly depressed. Pupils unequal in size; margins regular; reaction to light and accommodation prompt. Bladder slow; sexual power poor. Deep reflexes very active, more so on right side. Babinski and clonus present on right side.

Cerebrospinal Fluid

Date	Cells	Globulin	Wassermann	Gold Sol	Serum
12–18–15	45	3+	4+ 0·1 c. c.	5555542000	12–14–15 ++++
1–26–16	16	+	4+ 0·4 c. c.	5555432000	4–29–16 ++++
2–26–16	3	+	4+ 0·4 c. c.		8–23–16 −
3– 9–16	6	2+	4+ 0·4 c. c.	4444430000	3–10–17 −
4–19–16	7	2+	4+ 0·4 c. c.		11–24–17 −
5– 2–17	0	±	± 1·5 c. c.	1112332000	2– 2–18 −
6–13–17	2	±	2+ 1·0 c. c.		12– 5–18 −
7–27–17	2	±	3+ 1·5 c. c.	1123321000	3–29–19 −
3–16–18	2	±	4+ 2·0 c. c.		
4–24–18	2	±	3+ 2·0 c. c.	1122100000	
6–19–18	2	±	± 2·0 c. c.	1111000000	
3–29–19	2	−	− 2·0 c. c.	0000000000	

Treatment from December 29, 1915, to June 19, 1918: Eleven intravenous injections salvarsan; 17 intraspinal injections salvarsanized serum (Swift-Ellis, fortified with $\frac{1}{12}$ to $\frac{1}{4}$ mg.); 34 injections mercury; several courses of potassium iodide and mixed treatment.

Results: During the past year patient has been unusually strong and well. He has had no convulsions; his mental depression has disappeared and his memory is good. He takes an active interest in his work and is able to concentrate and apply himself to exacting legal work as well as formerly. His bladder has returned to normal and his sexual power has improved.

The hope of arresting the degenerative process lies in early recognition and a persistence in treatment. We are certainly justified by the results obtained in combating this serious type of early encephalitis by the most intensive methods at our command.

In the appended chart (Case IV) the amount and duration of treatments is shown. The patient is practically free from all mental or physical symptoms, is active in his usual vocation, and is only

aware of an abnormal state by reason of the persistent positive Wassermann reaction in the fluid. Are we justified in subjecting patients of this type to further treatment in the hope of reversing the Wassermann reaction, or must we rest satisfied with clinical cures and hope that time and the body defenses will cause the final disappearance of the reaction? A definite reply to these queries may be expected only after years of accurate observation.

Cerebrospinal Fluid

Date	Cells	Globulin	Wassermann	Gold Sol	Serum
12–12–13	26	2+	4+ 0·2 c. c.	5555554100	12–20–12 ±
6– 9–14	10	2+	4+ 0·4 c. c.		6– 9–14 ±
9– 9–14	8	2+	4+ 0·4 c. c.		12–21–14 ±
9–25–14	5	2+	4+ 0·4 c. c.		5–21–15 ±
10–21–14	3	2+	4+ 0·4 c. c.		9–10–15 ±
12–21–14	38	2+	4+ 0·4 c. c.	5555555420	1–12–16 –
1–15–15	30	2+	4+ 0·4 c. c.		3–14–17 –
4– 6–15	0	2+	4+ 0·4 c. c.		3– 6–18 –
5–21–15	1	2+	4+ 0·4 c. c.		1–15–19 –
7– 8–15	12	2+	4+ 0·2 c. c.	5555555420	
9–10–15	4	2+	4+ 0·2 c. c.		
10– 9–15	0	4+	4+ 0·2 c. c.		
11– 6–15	2	3+	4+ 0·2 c. c.		
12–15–15	3	3+	4+ 0·2 c. c.		
1–12–16	2	4+	4+ 0·4 c. c.	5555555420	
3–29–16	11	3+	4+ 0·4 c. c.		
4–26–16	9	3+	4+ 0·4 c. c.		
6– 3–16	8	3+	4+ 0·4 c. c.		
7– 8–16	12	2+	4+ 0·4 c. c.		
9–13–16	10	2+	4+ 0·4 c. c.		
10–24–16	19	3+	4+ 0·2 c. c.	5555555530	
12–20–16	18	3+	4+ 0·2 c. c.		
1–31–17	11	3+	4+ 0·2 c. c.		
3–14–17	12	4+	4+ 0·2 c. c.		
4–25–17	9	3+	4+ 0·2 c. c.		
6–16–17	5	4+	4+ 0·4 c. c.		
10– 3–17	38	4+	4+ 0·4 c. c.	5555555410	
11–21–17	3	4+	4+ 0·4 c. c.		
12–24–17	1	2+	4+ 0·4 c. c.		
3– 6–18	5	2+	4+ 0·4 c. c.		
4–17–18	5	+	4+ 0·4 c. c.		
7–24–18	6	2+	4+ 0·4 c. c.	5555555420	
8–22–18	4	2+	4+ 0·4 c. c.		
9–18–18	7	2+	4+ 0·4 c. c.		
10–30–18	14	4+	4+ 0·2 c. c.		
12– 4–18	9	4+	4+ 0·2 c. c.	5555543100	
1–15–19	5	3+	4+ 0·2 c. c.	5555543100	

Case IV. *Pre-Paresis.* (?) H., æt. thirty-eight. Chancre and secondaries skin and mouth in 1904. Internal treatment until 1910, when he developed left external rectus paralysis and suffered from shooting pains in legs and cramps in calves. In 1912 complained of tingling in legs. Came under observation in December, 1912. His reflexes were hyperactive, more so on right side; co-ordination perfect; no sensory changes; station and gait normal. Pupils regular in outline and equal; right slightly sluggish to light.

Treatment January 6, 1913, to January 15, 1919: 1 intramuscular injection salvarsan; 44 intravenous injections salvarsan; 69 intraspinal injections salvarsanized serum (Swift-Ellis, fortified with $\frac{1}{4}$ to $\frac{1}{3}$ mg.); several courses of mercury injections and potassium iodide and mixed treatment.

Results: Patient claims that he feels entirely well mentally and physically. He does the heavy work of an engineer and never loses a day except when he comes for treatment. His pupils and reflexes remain unchanged.

The Tabetic Group of Neurosyphilis. All syphilitic lesions are reactions to spirochætal invasion. In the skin and accessible tissues their evolution and regression can be followed and interpreted; secondary changes here, aside from deformity, are usually a matter of small moment. The central nervous system, however, presents more complicated problems in the results due to vessel occlusion and in tract degeneration secondary to focal lesions.

The clinical conception of tabes has been based largely on the results of degeneration in the posterior columns; namely, ataxia, loss of reflexes, sensory disturbance, and associated disorders of the bladder and sexual apparatus. In the preataxic stage, before any of the symptoms enumerated are fully developed and which may be present for years, modern methods of research often reveal conditions which are susceptible of relief by modern therapeutic agents.

The essential lesion in tabes is a posterior root and column degeneration with resulting death of the neuron, whether primary or secondary to a meningitis. The creation of a pseudo-tabes and a true tabes according to their theoretic mode of origin is largely artificial and based on few necropsy findings in the early stage of the process. A primary neuronal degeneration may occur and may be caused by direct invasion of the posterior roots and columns by the spirochætæ. The meningeal reaction in these cases may be absent or slight, and

may be secondary to the neuritis. The response to treatment in such cases would depend largely on when the condition is recognized and the accessibility to the spirochætæ of the specific drugs. But, if we are permitted to make any deductions from the fluid findings as to the character of the central lesion, we must conclude that in the majority of cases of progressive tabes meningeal reactions are present. Most of the earlier work is based chiefly on observations which antedated our exact knowledge acquired by biological examinations, and it is a matter of academic interest only as to which is the primary change. The intensity of the reaction, furthermore, is not necessarily dependent on the age of the process, as we have frequently found a cell count of over a hundred in tabes of twenty years' duration. Reactions of varying degrees of severity occur in all tissues which harbor spirochætæ; these may continue to multiply and involve new areas for an indefinite time. Advanced posterior column degeneration is of course irremediable, but many of the associated symptoms, as pain or crises, are due to an accompanying meningitis, and in so far can be relieved by treatment. Tabes progresses because the cause persists; new segments are involved by fresh invasions of the organism. It is clinically impossible to differentiate the so-called pseudo-tabes from its true prototype, as both have Argyll-Robertson pupils, absent deep reflexes, sensory disturbances, etc. Aside from symptoms from advanced degeneration in the lower segments of the cord, spinal fluid findings are a surer therapeutic guide than clinical symptoms alone. A tabetic with a relatively high cell count and other phases positive can be promised marked amelioration and probably arrest of his degenerative process. To call a case pseudo-tabes which responds to treatment and the other real tabes which shows no response is illogical. All the classical signs of tabes may be present in a patient whose spinal fluid shows active meningeal involvement, and these cases give the most striking improvement after treatment, as illustrated below:

Case V. *Tabes.* C., æt. forty-three. Chancre twenty years ago; secondaries denied. Treatment by inunction over a period of years. Was first seen in February, 1917, when he gave a history of having had shooting pains in his back and thighs, so severe at times that he was confined to his bed. He was nervous, irritable, and profoundly depressed, his mental condition interfering with his business activities. On examination he pre-

sented Argyll-Robertson pupils, ataxia, and sensory disturbance. The deep reflexes were absent in the lower extremities and sluggish in the upper. He had some bladder difficulty. For several months he had been intensively treated with salvarsan and mercury, but obtained no relief.

Cerebrospinal Fluid

Date	Cells	Globulin	Wassermann	Gold Sol	Serum
2– 7–17	243	4+	2+ 0·2 c. c.	3334430000	5– 5–17 –
2–14–17	179	4+	4+ 0·4 c. c.	3344441000	7–27–17 –
2–27–17	20	+	4+ 0·4 c. c.		1–30–18 –
3–14–17	10	+	4+ 0·4 c. c.	2333210000	
4–11–17	7	2+	4+ 0·4 c. c.		
5– 2–17	5	+	4+ 0·6 c. c.		
5–22–17	2	+	4+ 0·8 c. c.		
7–20–17	2	±	+ 1·0 c. c.	1123100000	
8–16–17	4	–	3+ 1·5 c. c.		
10– 6–17	3	trace	4+ 2·0 c. c.	1122100000	
11–10–17	1	±	± 2·0 c. c.		
1–30–18	2	trace	± 2·0 c. c.	1123210000	
3–23–18	1	±	+ 2·0 c. c.		
5– 4–18	1	–	2+ 2·0 c. c.	1122100000	
6–22–18	1	–	± 2·0 c. c.		
9–11–18	2	trace	– 2·0 c. c.		
11–20–18	1	trace	– 2·0 c. c.	1111000000	

Treatment from February 3, 1917, to November 16, 1918: 18 intravenous injections salvarsan; 19 intraspinal injections salvarsanized serum (Swift-Ellis, fortified with $\frac{1}{5}$ to $\frac{1}{2}$ mg.); several courses of mercury injections and potassium iodide.

Results: There has been complete disappearance of the pains and ataxia; he is no longer depressed and is able to conduct his business with his former energy. Bladder is occasionally slow. He has gained 25 pounds in weight and says his health is excellent.

In the tabetic group we may include (1) Arrested cases with Argyll-Robertson pupils, absent deep reflexes and anesthetic areas with a negative blood and spinal fluid. Several of these cases have been observed and controlled for three to five years with no clinical or serological change. Stationary or abortive tabes with a negative serology in its fluid is a contraindication to the use of intraspinal therapy. Salvarsanized serum is introduced into the spinal canal to combat active lesions. If the reactive phenomena are absent, it is fair to assume that the organisms have disappeared after causing a definite and limited lesion. The degeneration in question is non-progressive as a result of previous treatment or is spontaneously

cured by the normal defenses of the body. (2) Preataxic tabes with pupillary changes, absent or sluggish and unequal deep reflexes, bladder or sexual weakness, pains, and increasing fatigue in walking. Here we find a fairly high cell count, positive globulin, positive Wassermann reaction, and a luetic curve. The prognosis is relatively good, and we can predict arrest of the process with relatively little secondary degeneration. If permitted to progress would such cases become ataxic? Probably, as the symptoms point to posterior root or column involvement. (3) Advanced cases with ataxia, Romberg, bladder and sexual weakness, pains, crises, etc. The fluid may show a relatively low cell count with the Wassermann reaction positive in larger quantities, a positive globulin and a luetic, or it may be quite negative, curve. Intraspinal therapy offers less hope of relief in these patients because of advanced degeneration and the slight meningitis. In low tabes, too, there is danger of an added irritant to the cord and the possibility of an increase in symptoms. In these cases only the Swift-Ellis method should be used. In high tabes there is less inconvenience from the injected serum, and the treatment may be long continued with complete arrest of the process. (4) More or less advanced tabes, with a cell count varying from 20 to 100 or more, increased globulin, a positive Wassermann reaction in the high dilutions, and a paretic gold sol curve. These cases may or may not show mental symptoms, but offer an unfavorable prognosis as the reactions respond slowly to treatment if at all.

Case V. *Tabo-Paresis.* (?) M., æt. thirty-seven. Chancre and secondaries thirteen years ago. Treatment by mouth and inunction for three and a half years. For years has had lancinating pains in the legs and a sensation of numbness above the right knee. For several months had had dull frontal headaches; was easily fatigued and excited and was always very nervous. Examination revealed Argyll-Robertson pupils; ankle jerks absent; left patellar jerk absent, right very sluggish. No memory defect.

Treatment from July 23, 1917, to February 25, 1919: 21 intravenous injections salvarsan; 20 intraspinal injections salvarsanized serum (Swift-Ellis, fortified with ¼ to ½ mg.); several courses mercury.

Results: Clinically the pains have ceased and the patient is no longer nervous and has much more endurance. There has been no progress in his somatic signs.

CEREBROSPINAL FLUID

DATE	CELLS	GLOBULIN	WASSERMANN	GOLD SOL	SERUM
7–20–17	17	4+	4+ 0·2 c. c.	5555554200	7–20–17 ++++
8–23–17	8	4+	4+ 0·2 c. c.		2–20–18 +++
9–12–17	7	3+	4+ 0·2 c. c.	5555543100	7–24–18 ++
10– 3–17	4	+	4+ 0·2 c. c.	5555421000	12–11–18 +
11–21–17	4	2+	4+ 0·2 c. c.		
12–19–17	3	+	4+ 0·2 c. c.	5555431000	
1–23–18	4	2+	4+ 0·2 c. c.		
2–20–18	1	3+	4+ 0·4 c. c.		
3–27–18	3	+	4+ 0·4 c. c.	5555421000	
4–24–18	4	+	4+ 0·4 c. c.		
6–24–18	3	+	4+ 0·4 c. c.		
7–24–18	2	±	4+ 0·4 c. c.	5555431000	
10– 9–18	4	±	4+ 0·4 c. c.		
12–11–18	3	±	4+ 0·4 c. c.		
1–15–19	5	±	4+ 0·4 c. c.		
2–12–19	2	±	4+ 0·4 c. c.		
2–25–19	2	±	4+ 0·4 c. c.	5554421000	

The table on page 486 gives the serological findings in patients who presented the typical syndrome of tabes, i.e., Argyll-Robertson pupils, absent deep reflexes, sensory changes with ataxia and impairment of sphincter control.

The importance of the systematic examination of the eye grounds in all stages of syphilis should be emphasized by all teachers of syphilis, as pathological changes may be present with slight objective symptoms or visual impairment. The hope of preventing optic atrophy or arresting it in its early stages depends largely on such systematic examinations. Every case of optic atrophy, whether primary or a part of the tabetic or paretic syndrome, demands an examination of the spinal fluid at the earliest possible moment. This statement, in my opinion, admits of no argument. In case the spinal fluid shows a primary or associated meningitis with other positive phases of syphilis a method of treatment should be begun which offers hope of arresting the destructive process. Experience has shown how little may be expected from mercury, potassium iodide, or salvarsan intravenously. Persistence in methods demonstrated to be futile or of little value is wasted effort and time. The atrophy progresses and a stage is reached which admits of no relief. Theoretical objections to intraspinal therapy in cases which show the fluid findings of syphilitic meningitis are based on ignorance and

prejudice and closely approach criminal negligence. Intraspinal treatment in optic atrophy is indicated where the fluid shows a meningitis with the positive phases of syphilis. When present with other types of neurosyphilis the fluid findings may not accurately reflect the changes in the optic nerve or its meningeal coverings.

Serology in Tabes

	Cells	Globulin	Wassermann	Gold Sol	Serum
1—	60	++++	++++ 0·1	1123320000	−
2—	64	+++	++++ 0·4	1233210000	+++
3—	72	+++	++++ 0·4	4433210000	±
4—	73	+++	++++ 0·2	1123321000	++++
5—	73	+	++++ 0·4	1123210000	++++
6—	75	+++	++++ 0·5	2233210000	+
7—	81	++++	++++ 0·4	2321000000	−
8—	93	++++	++++ 0·2	1122321000	−
9—	100	++++	++++ 0·2	5555542000	++++
10—	120	++++	++++ 0·1	2223310000	++++
11—	150	+++	++++ 0·1	5555543000	++++
12—	150	++++	++++ 0·2	1123210000	+++
13—	172	+++	++++ 0·2	5555543100	+
14—	175	+++	++++ 0·4	1123320000	+
15—	175	++++	++++ 0·1	1233210000	++++
16—	175	++++	++++ 0·2	1123221100	++++
17—	193	++++	++++ 0·2	3333343100	++++
18—	230	++++	++++ 0·1	1233210000	+++
19—	247	++++	++++ 0·2	1123321000	−
20—	268	+++	++++ 0·2	5555431000	++
21—	315	+++	++++ 0·2	5555543100	+

N. B.—The cases with the paretic curve and strongly positive Wassermann reaction are potentially tabo-paresis. None of these cases, however, had clinical indications of mental involvement at time of examination.

The optic atrophy is, however, the condition which calls for immediate relief. The integrity of an important organ is involved and admits of no delay in futile efforts. In advanced atrophy with negative or practically negative findings in the fluid little can be expected from treatment of any kind. Persistent intraspinal treatment, when indicated by the fluid findings, can arrest the progress of many cases and preserve the remaining vision. Theoretical arguments that the serum does not reach the invaded nerve are invalidated by the results of treatment. Employment of a proper technique medicates outside the spinal canal one-third of the entire spinal fluid when this is returned by gravity. Salvarsanized serum directly

introduced into the lumbar subarachnoid space diffuses itself more slowly and accomplishes less than when diluted outside the body with a large quantity of fluid.

The results obtained in cases like the following overthrow the contentions of those who oppose the treatment because of physiological arguments.

Case VII. *Optic Atrophy and Tabes.* B., æt. forty-five. Syphilis and gonorrhea denied. In January, 1917, he gave the following history: For thirteen years had had intermittent attacks of severe shooting pains and for two years similar pains in the chest and upper extremities. Four years ago nervous breakdown with suicidal tendencies. Bladder and sexual weakness for three or four years. Impairment of vision for two years. When first seen could only distinguish light and dark with the right eye and could only read large print with the left. Pupils were unequal, irregular, and gave the Argyll-Robertson reaction. All deep reflexes upper and lower extremities were absent.

Cerebrospinal Fluid

Date	Cells	Globulin	Wassermann	Gold Sol	Serum
1–12–17	63	3+	4+ 0.2 c. c.	5554431000	1–10–17 +++
2–17–17	9	2+	4+ 0.4 c. c.		1– 5–18 ++
3–31–17	7	+	4+ 0.6 c. c.	1133310000	1–23–19 ±
4–25–17	5	±	2+ 0.6 c. c.		
5–29–17	6	+	4+ 0.8 c. c.		
10– 9–17	3	+	± 1.0 c. c.	1123210000	
11– 3–17	5	+	3+ 1.5 c. c.		
1– 9–18	3	±	± 1.5 c. c.	1123210000	
2–20–18	1	trace	+ 1.5 c. c.		
3–13–18	2	±	2+ 2.0 c. c.	1123210000	
4– 6–18	1	–	4+ 2.0 c. c.		
5–25–18	3	trace	4+ 2.0 c. c.	1123210000	
6–22–18	2	trace	3+ 2.0 c. c.		
9–28–18	2	trace	2+ 2.0 c. c.		
10–26–18	3	trace	2+ 2.0 c. c.	1112100000	
1– 4–19	2	trace	± 2.0 c. c.		
1–29–19	0	trace	– 2.0 c. c.	1112100000	

Treatment from January 15, 1917, to February 26, 1919: 22 intravenous injections salvarsan; 23 intraspinal injections salvarsanized serum (Swift-Ellis, fortified with $\frac{1}{10}$ to $\frac{1}{2}$ mg.); 32 injections mercury and courses of potassium iodide.

Results: Pains, nervousness, and suicidal tendencies have disappeared; his bladder has become normal and his sexual power has improved. He

states that the vision in his right eye is somewhat better and that of the left eye considerably more acute than two years ago. From the ophthalmologist's report the vision in his right eye is 3/200 and in his left 18/40.

Paresis is readily diagnosticated when degeneration of the brain cells is sufficiently advanced to cause marked mental symptoms—disorientation, speech disturbance, expansive ideas, and convulsions. The blood and spinal fluid in these cases practically always yield a strongly positive Wassermann reaction, the latter in high dilutions in the spinal fluid with a strong globulin content and a gold sol paretic curve. The number of cells in the fluid is variable; in treated cases the cells may amount to twenty or less. In the majority of fluids examined the cell content is the first of the phases to be influenced by treatment. Where intensive courses of salvarsan intravenously have been given before lumbar puncture was made a low cell count is often found, but not always.

The data accumulated as to the average period when paresis occurs after the primary infection are based largely on the time when obtrusive symptoms appear. Psychiatrists and neurologists, as a rule, see cases only in this stage, and have little or no experience with patients showing vague or transitory symptoms which may have been present for years previously and wrongly interpreted. Although the literature of psychiatry often recites the occurrence in the previous history of paretics of neurasthenic states and passing symptoms indicating mental disturbance, little weight has been attached to them by the patient or his medical adviser.

Since systematic examination of the spinal fluid in early syphilis too little time has elapsed to enable us to speak with certainty as to the type of early neurosyphilis which may develop paresis. We have, fortunately, spinal fluid tests which indicate the probable site of the syphilitic infection in the central nervous system and a large number of examinations showing to what degree these reactions resist therapeutic attacks which influence the more superficial types of neurosyphilis. Accurate clinical and serological observations over a period of five years in certain of these cases have developed a considerable degree of confidence in the prognostic value of the tests. A spinal fluid which shows a positive Wassermann reaction in the lower dilutions with a luetic gold

sol curve is of favorable prognostic import as regards the possible development of paresis. On the contrary, the persistence of the Wassermann reaction in the high dilutions with a paretic curve is of graver significance.

The probable development of paresis should always be kept in mind when little or no impression can be made on the Wassermann reaction in the spinal fluid by persistent intraspinal treatment. Symptoms due to the coexisting meningitis or to lesions in the superficial layers of the cortex may disappear and remissions of longer or shorter duration be induced by treatment, but as to the possibility of permanent cures in deep-seated encephalitis little of a positive assertion can be made. Limited involvement of the brain may exist for years with little effect on the intellectual processes, and show the spinal fluid findings of paresis. The progress of such cases is slow, and they may appear normal in every respect. Potentially paresis is present in them and only long-continued observations controlled by laboratory tests can reveal the final outcome. Intraspinal treatment modifies the course of well-developed paresis and often renders the individual capable of resuming his activities for a time.

Case III. *Paresis.* K., æt. forty-five. Syphilis denied; gonorrhea fourteen years ago. Was first seen September 13, 1917, when he exhibited delusions of grandeur, speech disturbance, and memory defects. His employer had complained of his carelessness and inattention to work for the past several months. He frequently fell asleep at his desk. On examination he was found to have rigid pupils, hyperactive reflexes, facial tremor and writing defects. His sphincter control was normal; he gave a history of perverted sexual desires for several months.

Treatment from September 13, 1917, to February 12, 1919: 29 intravenous injections salvarsan; 23 intraspinal injections salvarsanized serum (Swift-Ellis, fortified with $\frac{1}{5}$ to $\frac{1}{2}$ mg.); several courses of mercurial injections and potassium iodide.

Results: His mental condition is totally different. He has lost his delusions of grandeur and his speech has improved so that he is able to make long addresses without difficulty. For eight months he has been carrying on trying war work without inconvenience. He has no gross memory defects, but his wife says he is forgetful at times. Sexually he has returned to normal.

Cerebrospinal Fluid

Date	Cells	Globulin	Wassermann	Gold Sol	Serum
9–15–17	80	4+	4+ 0·2 c. c.	5555542000	9–15–17 ++++
10–13–17	16	4+	4+ 0·2 c. c.		5–25–18 ++++
11–10–17	10	4+	4+ 0·2 c. c.	5555431000	1– 8–19 ++++
12– 8–17	8	3+	4+ 0·2 c. c.		
1–26–18	7	3+	4+ 0·2 c. c.		
2–20–18	7	2+	4+ 0·2 c. c.	5555421000	
3–30–18	3	+	4+ 0·2 c. c.		
4–27–18	3	+	4+ 0·2 c. c.		
5–18–18	2	+	4+ 0·2 c. c.	5555431000	
7–12–18	3	±	4+ 0·2 c. c.		
8–14–18	2	±	4+ 0·2 c. c.	5555421000	
10– 2–18	2	±	3+ 0·2 c. c.		
11–13–18	1	±	4+ 0·2 c. c.		
12–11–18	4	±	4+ 0·2 c. c.		
1– 8–19	2	±	4+ 0·2 c. c.	5555431000	
2–12–19	1	±	2+ 0·2 c. c.	5555431000	

The remission in symptoms is doubtless due to the control of the meningitis and more superficial lesions. The continued activity in the deeper lesions leads to slow degeneration of the brain cells and ultimately to complete dementia and death. Reports made from time to time regarding rapid changes in the Wassermann reaction and the gold sol test by intraventricular or other treatment are based on limited observations and incorrect laboratory tests.

The results obtained by the intraspinal treatment in pre-paresis when sufficiently prolonged at times are so encouraging that we feel justified in carrying it out to the limit of the patients' endurance. They are entitled to the only procedure which offers any hope of benefit if it is unattended by risk. We feel that with the careful technique now employed and with the proper preparatory treatment that danger to the patient's life or possible damage to the cord or brain has been entirely eliminated. Such treatment by the inexperienced without laboratory facilities and proper serological control will certainly fail and cause the procedure to be condemned as useless and harmful.

UNUSUAL REACTIONS TO TYPHOID–PARA–TYPHOID VACCINATION

By Nellis B. Foster, M.D., Washington, D. C.

THE reaction which is usually experienced from prophylactic doses of typhoid vaccines amounts only to a slight discomfort. At worst the subject is seldom more uncomfortable than he would be with an acute tonsillitis, and he has the consolation that eighteen to twenty-four hours will mark the termination of the symptoms. There seems to be a consensus of opinion, however, that vaccination with the mixed typhoid-para-typhoid culture is not so apt to be passed unnoted as vaccination with the single typhoid strain. The symptoms, commonly varying somewhat in degree, are slight fever, chilliness, muscular pains, and backache; not so usual, but still relatively frequent, are severe headache, vomiting or diarrhea, or both, epistaxis, and bronchitis, which last may continue for days or even a couple of weeks. This list includes all the symptoms which occur in the average cases, and from these deviations are not usual. Occasionally, of course, bizarre cases are noted, due, perhaps, to some accident in technic.

Differentiated from the above-mentioned majority, of over 40,000 vaccinated troops, was found a group of cases admitted to the wards of the Base Hospital at Camp Meade on account of rather severe symptoms. These symptoms at least suggested certain specific diseases. On account of the diseases simulated this group may be subdivided into meningeal, appendical, and purpuric types. These cases were sufficiently frequent to afford opportunity for study, and because of the diagnostic embarrassment which we experienced in the beginning, no little attention was given to them. The reaction which bore resemblance to appendicitis was most common. At least fifty of these cases were studied, and of the other types a somewhat smaller number.

The meningeal type of reaction is alarming because of the resemblance to meningitis. When, as happened with two cases, there

were in addition to other signs a few fine purpuric spots on the body, the resemblance to an early stage of "spotted fever" was complete. The usual course of events with my cases was initiated by headache, commencing a few hours after vaccination and gradually increasing to an almost unbearable intensity. With severe headache photophobia is the rule. There was pyrexia up to 102° F. and sometimes vomiting. When put in bed the patient assumes the meningitis posture—lying on the side, knees up, and head thrown a little back. On examination one finds invariably with these cases some stiffness of the neck, a positive Kernig sign and mild hyperesthesia. In the absence of history, diagnosis can hardly be made without lumbar puncture. When lumbar puncture is done the cerebro-spinal fluid is found under considerable increase of pressure, often dropping too fast to be counted. The fluid is clear and normal. There is no significant cell increase. Withdrawing 10–15 cu. cm. of fluid almost invariably relieves the headache. In brief, the condition is one of meningismus.

The appendicitis picture is definite enough as a clinical picture with localized pain and tenderness, slight fever, and some increase in the leucocyte count (due to the vaccine). A number of these cases were operated upon. The appendices removed, however, did not present the conditions expected, and an agreement between the surgeon and the pathologist on this point was impressive. With this experience a conservative attitude developed and none of the cases of this type was operated upon. At a somewhat later period, while at General Hospital No. 14, I found that Lt. Col. Edward Martin had become interested in the surgical aspect of this problem, but had come to a different conclusion in that with his cases the appendix did show more evidence of acute inflammatory change. Col. Martin's cases gave histories suggesting repeated attacks of appendicitis in the past, and it has been proposed in explanation that the vaccination excited an acute process in an individual thus predisposed. Neither the immediate practical question involved nor the underlying one of scientific principle can be clarified by evidence now available. It will be recalled that shortly after typhoid vaccination began to be somewhat extensively used among our civil population in the cities, the statement was made and repeated that latent tuberculous foci in the lungs might be thus fanned into

activity. Some scattered attempts were made to ascertain the truth, but these studies bear analysis as badly as the statements to be examined. At present there are opinions, but little evidence. Similar opinions are current as to the effects of vaccination on latent chronic urethritis, arthritis, and some other conditions. The whole subject requires careful re-examination. It is of interest in passing to recall that vaccines made from typhoid cultures have been advocated for the treatment of some of these conditions—arthritis, urethritis—which we are now assured are aroused into activity by the same measure.

There is so much obscurity surrounding the etiology of purpura that the cases following vaccination had for me an especial interest. The first of these cases to receive recognition was admitted from a Regimental Infirmary on account of epistaxis. He had been vaccinated the day before admission and there was the usual mild reaction. On the morning of admission to hospital he had epistaxis and for this reported at sick call. The epistaxis was obstinate and required "packing." Examination showed a purpuric eruption covering the body. The spots were small and discrete, varying from $\frac{1}{16}$ inch to $\frac{1}{8}$ inch and purplish in color. There was no bleeding of the gums; no blood found in urine or feces. We had not at this time facilities for exact measurement of the clotting time, but no abnormality was noted by means of improvised apparatus. The bleeding time and cell counts were normal. The rash gradually faded to a tawny-brown stain and the patient was returned to duty.

On inquiry, stimulated by this case, it was found that a number of cases had been admitted to the Otology service of the hospital because of epistaxis following vaccination, and that it had been recognized that many of these had hematuria and a few had purpuric eruptions. A number of cases of varying degrees were studied subsequently in both these services. Epistaxis with transient hematuria was not uncommon. Some of these showed also hemorrhages and purpuric rashes. In one case there was violent epistaxis, hematuria, melena, an extensive purpura and hemorrhage into some of the joints. The left elbow had later to be opened and the clot removed. All of these cases made perfect recoveries.

Since an understanding of this condition would be helpful for an understanding of purpura, examinations were made of the blood

in respect to the clotting and bleeding times, cell counts, and platelet counts. So much normal variation was found in the platelets that no evidence could be secured in this direction. The other estimations were normal except a slight leucocytosis observed in many cases after vaccination without special symptoms.

With all of this group of unusual reactions, purpuric included, it seems necessary to postulate an idiosyncrasy. With the purpuric group, histories were examined with care, but fruitlessly. There was not one who had come from a family of bleeders, for example. Perhaps the more on this account, the production of purpura in some individuals may help to clarify the problem of simple purpura. That it can be induced by bacterial derivatives is alone significant.

VISUAL DISTURBANCES IN POLYCYTHEMIA VERA

By Harry Friedenwald, Baltimore, Md.

SIR WILLIAM OSLER in 1903 described "Chronic Cyanosis with Polycythemia and Enlarged Spleen." (1) He reported four cases which had come under his own observation and noted in one of them: "Both disks hyperemic. Retina surrounding disks thickened. Vessels, particularly veins, enlarged and tortuous," and in another, "failing vision, the condition of the fundi was negative with the exception of tortuosity of the vessels."

These were the first observations bearing upon changes in the eye-grounds and upon defects of vision in this disease.

During the fifteen years that have elapsed since Dr. Osler's article appeared many cases of Polycythemia have been described. In 1912 Lucas collected 189. (2) In spite of "the eye being mentioned in only forty-four cases (30 per cent), and an ophthalmoscopic examination having been made only in twenty-six cases (18 per cent), disturbances of vision were reported in thirteen cases," one of these becoming quite blind, "although nothing was found in the optic disks beyond slight hyperemia and enlargement" (Hutchinson and Miller); another "had blurring of vision and occasional diplopia; the veins of the fundus were markedly tortuous and dilated and the retina edematous and deeper red than normal" (Parker and Slocum); another case had "blurring of vision and diplopia; . . . Vision O. D. $\frac{6}{7.5}$, O. S. $\frac{6}{9}$, retina hyperemic, veins much engorged, tortuous and dark in color" (Parker and Slocum); still another showed "dilatation of the retinal veins, decreased vision, unimproved by any lens and a slight rotary nystagmus" with a very unusual change in the appearance of the nerve head (Hall and Jackson); blurring of vision was observed with engorgement of fundus (McKeen, Watson-Wemyss); and without description of fundus (Weintraud, Anders). Hazy vision with choked disk (Lucas), sudden darkening of vision (Kaester-Jackson), flashes of light and photophobia (Nicola), dimness and finally blindness

with optic neuritis (Purves Stewart), were noted in other cases. Blurring of the optic disks, enlarged and tortuous vessels, discoloration of the eye-grounds, retinal hemorrhages, and typical choked disks were observed in a number of cases, without mention of visual disturbances.

However, it is not to the fundus lesions, which are well known, that the writer desires to draw attention, but rather to the visual disturbances which sometimes accompany them and at other times occur independently or in association with fundus changes too slight to account for them.

The only observations which I find bearing upon visual impairment that have been published since those just referred to are to be found in Christian's article on "The Nervous Symptoms of Polycythemia Vera." (3) Christian describes ten cases. Visual defects are mentioned in the following:

Case I: "Attacks of transient blindness; at other times blurring of vision . . ." Case III: "Disturbances of vision, although repeated eye-examinations have shown no visual defect. . . . " Case IV: "For ten years, eye symptoms consisting of fatigue and poor vision, scintillating scotoma, and blind spots in field of vision . . . left homonymous hemianopsia; edema and hyperemia of optic disks . . . " From a personal communication from Dr. Christian, I learn in this case, that ten years prior to the final illness in 1905 there was dyslexia; "the interior of the eyes were normal, and there was not the least suggestion of neuritis except that the veins were a good deal congested." "On September 30, 1915, Dr. C. B. Walker of the Brigham Hospital makes this note: Left homonymous hemianopsia is pretty definitely demonstrated by using a weak ophthalmoscopic light, and seems to be fairly sharply vertical." Case V: "Optic disks showed slight blurring." Case VI: "For ten years . . . black spots before . . . eyes moving laterally (ophthalmoscopic examination shows numerous opacities in the vitreous) . . . trouble in vision . . . " "Flashes of light before . . . eyes and scintillating scotoma seen to the right." Case VIII: "For ten days blurred vision and diplopia . . . " Case IX: "Blurred vision for three days . . . paralysis of the left external rectus muscle of the eye . . . " Case X: "There were no eye symptoms beyond slight fatigue and occasional blurring. . . ."

In these cases we are struck by the frequency of the visual disturbances as well as by their indefinite character. It is unfortunate

that while the number of observations concerning disturbances of vision is not inconsiderable, the cases were not studied specially from the ophthalmological point of view and fields of vision were not recorded.

The case which I desire to report is interesting from the fact that the visual impairment was the chief, indeed, the only symptom of importance resulting from polycythemia. The patient, a physician, aged twenty-nine, first came under my observation on April 8, 1914. He informed me that he had trouble in his right eye which had begun two years previously after exposure in surveying. He had suffered with headaches. His chief disturbance at that time consisted in failing vision after looking at an object for some time. His vision had been reduced, but had been improved before I saw him. He informed me that he had undergone careful examinations and no general organic trouble had been found. He regarded himself in perfect health.

The pupils were equal and reacted normally; the right optic disk was very hyperemic and the outlines were entirely lost. The left disk was also somewhat hyperemic, but the outlines were more defined; otherwise the fundi of both eyes were normal.

Suspecting optic neuritis, I examined the central and peripheral vision very carefully; the fields of vision for form and color were perfect; the blind spots were accurately outlined; they were oval, with the long axis vertical, the left 6° x 7°, the right 8° x 9°. His central vision with correcting glasses was perfect as follows:

O.D. + 1.25 D. S. = − 0.25 Dc. Axis 180 V. = 20/15; O. S. + 1.5 = 0.75 Dc. Axis 180 V:=20/15.

I prescribed these glasses and he found them comfortable and continued his work.

I examined him a number of times; in May and December, 1914, in November, 1916, and his vision was always normal; indeed it was more than normal, I recorded 20/12 and even 20/9 at times.

Under the circumstances stated I was forced to the opinion that the ophthalmoscopic picture did not indicate the presence of optic neuritis, but was that of a pseudo-neuritis.

It should be stated that during this period he observed increasing growth of the thyroid. Slight enlargement of the left lobe of his thyroid first became apparent in 1907; and then progressed slowly without symptoms, until the spring of 1915. From that time until the summer of 1916 the increase in size was rapid; and attacks of paroxysmal tachycar-

dia and arrythmia developed, which gradually increased in frequency. At the same time, loss of some twenty pounds in weight occurred; slight exophthalmos developed; and during the winter of 1915–16 he had several attacks of migraine with characteristic scintillating scotoma. He was advised to submit to operation. In July, 1916, left lobectomy was performed and was followed by gradual relief of all symptoms, the tachycardia being the last to disappear. Extrasystolic arrythmia has persisted. The pathologist reported the tumor as an encapsulated adenoma surrounded by a very thin layer of normal gland tissue.

In June, 1917, the tonsils were enucleated following an attack of infectious arthritis, which promptly cleared up.

After a long interval I again examined the patient on May 2, 1918, when he returned on a furlough from the medical service of the army. He informed me that his health had been good, he had been under a heavy strain, doing excessive eye-work, and that during January, 1918, his vision had failed. On May 2d I had the opportunity for only a brief examination and found vision in each eye 20/48, slightly better in the right eye. On May 9th I examined him again and found vision 20/48 in each eye, slightly poorer in the right, a very great drop of vision when compared to the remarkable acuity he had in previous years. The fields of vision showed slight concentric contraction; for form the contraction was between 5° and 12° in the left, and from 10° to 20° in the right; the color fields for the red were contracted from 10° to 20° in both fields. There were no central or paracentral scotoma, absolute and relative, for white or colors.

The ophthalmoscopic appearance of the eye-grounds was unchanged; it was exactly as it was in previous years. The absence of a central scotoma excluded toxic amblyopia from the use of tobacco or alcohol, neither of which was indulged in excessively. I was therefore in great doubt in regard to the diagnosis. I felt sure that his slight thyroid trouble played no part. It should be stated that no ocular signs were visible. There was neither exophthalmos nor von Graefe sign. In the absence of any assignable cause I was inclined to regard his condition as hysterical. I urged further and complete physical examinations, which failed to discover any satisfactory explanation, and finally had him submit his case to Dr. Lewellys F. Barker, who found that the patient had polycythemia rubra vera and that this accounted for his visual trouble. From Dr. Barker's note under date of June 3, 1918, I take the following:

Patient is well nourished. . . . No nasal obstruction. Mucous membranes good color. There are a number of suspicious teeth; some retraction of the gums. Some tonsillar tissue on the right side which is slightly tender.

There are no glands at the angles of the jaws; glands in the posterior triangles are not large. Has scar at the base of neck, mostly on the left side, very inconspicuous. The thyroid isthmus is a little thick, no nodules felt. There is slight tremor of the fingers, more in the left hand; hands are rather short and broad. Radial pulses are synchronous, 22 to the quarter; radials are not especially thickened. Epitrochlears are palpable. Blood pressure 130/90. Heart is not increased in size, practically negative. There is no special accentuation of any sounds. Lungs clear front and back. Slight tenderness in the lower portion of the abdomen, as much on the left as on the right. Liver edge not felt. Spleen not felt. No masses made out anywhere. Has had pain in gall-bladder region in recent months. Abdominal reflexes very active. Deep reflexes in the arms are rather sluggish; knee kicks are equal, obtained with reinforcement. Marked tickle response on plantar stimulation. There is no edema.

Blood Examination

R.B.C.	6,400,000	
Hb	115 per cent	
W.B.C.	9400	
P.M.N.	163	65.2
P.M.E.	3	1.2
P.M.B.	2	.8
S.M.	67	26.8
L.M Tr	15	6.0
	250	100.0

R.B.C. and platelets normal. Most of the lymphocytes are of the large-celled variety.

Blood, Wassermann Reaction:

Antigen A, cholesterinized human heart, negative.

Antigen B, acetone insoluble lipoids, negative.

Antigen C, plain extract beef heart, negative.

It is to be noted that there were no other signs or symptoms of polycythemia, aside from the evidence of the blood examination.[1]

I had the opportunity for subsequent examinations on June 17, 1918, when vision appeared slightly improved, vision O.D. 20/38, O.S. 20/30

[1] A later examination of the blood was made by Dr. Charles E. Simon on December 11, 1918, who reported the following: R.B.C. 6,080,000, Hb. 106 per cent, W.B.C. 9350. P.M.N. 56, P.M.E. 1.5, P.M.B. 0, S.M. 36 per cent, L.M. and Tr. 6 per cent. The blood does not show increased degree of viscidity. Morphologically examined, red cells show no abnormality. There are no stipple cells and no polychromasia. The blood platelets are not increased.

and June 28th vision O.D. 20/48, O.S. 20/30. I examined the fundi on each occasion and found no change. The patient has been enjoying good health and has continued with his military medical duties. There are no ocular evidences of thyroid disease. His color is healthy. The bulbar conjunctiva is not congested. The last examination was made on December 12, 1918. Central vision with his correcting glasses O.D. 20/48, O.S. 20/24 almost. The fields of vision are still slightly contracted for form, but not as markedly as in May, 1918. The color fields still are contracted as noted in May, 1918. The blind spots are slightly oblong vertically and slightly enlarged in the left 7° x 9°, in the right 8° x 9°.

The appearance of the eye-grounds is unchanged. From my notes I take the following:

"The disks are markedly congested, their color being little different from that of the surrounding retina. The outlines of the left disk can be made out on the temporal side and less distinctly on the nasal, but not above and below. The congestion of the right disk is even more marked than that of the left, so that the excavation of the left shows some whiteness, that of the right is quite red. The outlines of the right disk can be made out only on the temporal side and indistinctly. The blood vessels are quite healthy, show no tortuosity; the arteries run in rather straight lines, are full, but not over distended, and arteries and veins present bright reflexes."

The case emphasizes the importance of the visual symptoms in the disease we are considering, as well as their occurrence in very mild cases. The transient visual disturbances which had occurred years before the present attack, the long interval of perfect visual function and the recent recurrence of marked and persisting visual impairment, associated with an unchanging picture of optic neuritis made the case very puzzling. When the patient was seen in 1918 with vision reduced, without any evidence of underlying disease, and without any alteration in the appearance of the eye-grounds, I was inclined to consider the trouble purely functional, hysterical in character. This seemed to be confirmed by the contracted fields of vision. It was only after Dr. Parker examined the patient and discovered the polycythemia that the solution of the puzzling condition was found.

The interpretation of the ocular affection and of the visual defect, however, present no inconsiderable difficulties. The diagnosis of mild optic neuritis cannot be accepted unhesitatingly in view of

the unchanging fundus picture during four years of observation, during periods of marked change in visual function.

The slight enlargement of the blind spots points to the disks as the seat of lesion. Accepting this view involves admission that a very mild polycythemia may cause serious congestion of the optic disks with mild neuritis lasting a number of years. But we must also concede the possibility of a retrobulbar perineuritis which may account for the contraction of the fields.

The cause of the nerve lesions lies in the "increased viscosity of the blood which favors the stasis and capillary enlargement." (4) Edema, hemorrhages, and inflammatory processes result. Behr (5) who had the opportunity to make microscopic examination of the ocular lesions, explains the process as a consequence of vascular changes; the vessels lose their elasticity, their surface is increased, the circulation is retarded, and the plasma passes into the surrounding tissues. When the lymph vessels no longer suffice to carry it off there is lymphatic congestion, resulting in optic neuritis. If this increases, choked disk occurs, similar to that due to increased intra-cranial pressure.

But whether the visual impairment in the case described be due to a retrobulbar neuritis or to a papillary neuritis it is evident that such conditions do not explain some of the cases that have been described. The visual disturbances associated with choked disk in polycythemia are doubtless to be explained in the same manner as in choked disk due to the more common cause, increased intracranial pressure. Still other cases owe their visual impairment to cerebral lesions (hemiopia), or to paralysis of the extrinsic muscles with resulting diplopia.

In view of the lack of any satisfactory treatment of polycythemia, no suggestion can be offered concerning the treatment of the ocular affections which result from it.

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ADVANTAGES AND LIMITATIONS OF THE ROENTGEN RAY IN THE DIAGNOSIS OF GASTRO-INTESTINAL AFFECTIONS

By Julius Friedenwald, M.D.,

Professor of Gastro-Enterology, University of Maryland, School of Medicine and College of Physicians and Surgeons, Baltimore, Md.,

and

F. H. Baetjer, M.D.,

Associate Professor of Clinical Roentgenology, Johns Hopkins University and Hospital, Baltimore, Md.

THE great difficulties arising in the diagnosis of many gastro-intestinal disturbances have long been recognized. In spite of our most thorough means of investigation, including the use of the latest and most accurate methods, the diagnosis of many of these problems often remains obscure, and is indeed at times impossible.

With the advent of the roentgen ray new light has been shed upon many of these intricate problems, and in consequence new and important facts in diagnosis are more frequently cleared up. While the roentgen ray has been of the greatest aid in solving many of these important questions, and from what has been accomplished it seems quite probable that as the technic of roentgenology and our method of interpretation of the *x*-ray plates become more perfected, that many unsolved difficulties in gastro-enterologic diagnosis will be cleared up; yet it must be remembered that this method is only a single means of examination, and must not be relied upon alone, and that only when taken in connection with the other clinical signs does it attain its greatest value.

While the *x*-ray is of the greatest diagnostic help in solving difficult problems in gastro-enterology, there are limitations as to the conclusions which may be drawn from this method of diagnosis, and indeed in a small percentage of cases the results may at times

even become misleading. This is not due, however, to the fact that the *x*-ray does not present actual conditions, but is caused by certain limitations in our technic as well as by the difficulty frequently encountered in the proper interpretation of the shadows on the plates.

Much has been written concerning the great value of the *x*-ray in the diagnosis of gastro-intestinal disturbances, but little has been brought forth regarding its limitations. It therefore seems timely that the limitations of this method of examination should be definitely noted, for while we fully recognize that many of these difficulties will in time be overcome, yet at present we are anxious to emphasize the fact that in this method we possess but a single form of examination which cannot be relied upon alone, but when taken in connection with the other clinical signs is of the greatest diagnostic help.

Ulcer of the Stomach and Duodenum. It is a well-known fact that the roentgen ray is of the highest diagnostic aid in revealing ulcers of the stomach and duodenum, and yet in some instances these lesions are not revealed by this method of examination, or defects may be present which are interpreted as ulcerations which cannot be detected at operation. In explanation of these facts it might be said that ulcers situated in certain locations in the stomach and duodenum may not be revealed by the *x*-ray. Only when the lesion is situated on the anterior surface of the stomach and along the anterior surface of the lesser and greater curvatures are they revealed. Yet, according to our observations the functional signs are often as important as the presence of a defect in arriving at definite conclusions as to the presence of an ulcer. It is therefore of the greatest importance to bear in mind the value of the functional signs in diagnosis, even though a defect or deformity may be absent in repeated examinations. Thus in 8 per cent of cases studied by us there were no defects observed, yet the functional activity of the stomach pointed definitely to ulcer. However, in a certain number of cases there are definite clinical evidences of ulceration, and yet the *x*-ray presents no indication whatever of this condition. This may be due to adhesions—to which attention will be called later on—masking the true condition, but the absence of definite *x*-ray signs cannot always be traced to this factor.

It happens at times that a complicating appendicitis or cholecystitis may be so marked as to mask any findings in the stomach itself, and the significance of a small filling defect might easily be overlooked.

In one of our cases (Dr. B.) a man of sixty-four years of age who had presented definite clinical signs of ulceration for years, and in whom the *x*-ray findings had been positive four years previously, was again examined. The *x*-ray examination showed a mass of adhesions in the upper right quadrant region, involving the duodenum and gall bladder. The duodenum was fixed and deformed. The *x*-ray diagnosis was that of adhesions and it was impossible to determine whether the deformity was due to an ulcer or to adhesions. The operation showed a large duodenal ulcer with adhesions.

In another instance (Mrs. B.) the *x*-ray findings pointed to a chronic appendix with a very spastic, irritable stomach, and no defects could be made out. Consequently the *x*-ray conclusion was that the condition was simply that of a reflex stomach, but at operation besides a chronic appendix there was an ulcerative lesion in the duodenum.

In a large series that were examined, in 3 per cent of the cases of ulceration no filling defects could be made out by means of the *x*-ray examination; and in 15 per cent of the cases the symptoms were not definite enough to make an absolute diagnosis of ulcer. It is especially in those instances in which there is marked evidence of chronic appendicitis or cholelithiasis with adhesions that ulcer of the stomach or duodenum may be present, and yet not be revealed. On the other hand, one cannot at this time pass by another group of cases in which the ulcerations are of the so-called mucous type. These are easily demonstrated by means of the *x*-ray, but are rarely observed at operation unless the stomach or duodenum is actually opened. It has been our experience in a number of instances of this kind that when an exploratory operation was performed and the stomach and duodenum palpated, no ulcer was observed; the symptoms, nevertheless, would persist, and these cases would later present such definite signs that for the relief of the symptoms a second incision was indicated when the ulcer was revealed. In one such case (Miss F.) the operation revealed absolutely nothing abnormal. The patient was temporarily relieved, but returned at the end of six months, presenting all of her former symptoms. A second

x-ray examination disclosed almost a complete gastric obstruction. The second operation exhibited a large indurated ulcer in the pylorus with scar formation. The former examination had pointed to ulcer at the pylorus, and since it could not be palpated at operation it was overlooked. There cannot be any question that many ulcerations of this type are passed by unnoted at operation. The greatest difficulties arise in the diagnosis of complicated cases; that is, when adhesions are present, due either to the healing of the ulcer or to inflammatory conditions involving one or other of the organs in the abdominal cavity. These adhesions so frequently mask the usual findings that it is often impossible to determine whether we are really dealing with an ulcer or whether a lesion of some other organ is causing the symptoms. Such adhesions may arise from the ulcer itself, from the gall bladder or appendix, or there may be no adhesions at all in the region of the stomach, and the gastric findings may be due to a purely reflex condition or to spasm.

It is necessary at times, in a certain proportion of cases in which adhesions of the stomach are present, to lay special stress upon the clinical history of the case before a final decision can be made. If the clinical signs coincide with a definite history of ulcer, we must conclude that the adhesions have taken their origin from the ulcer; if of cholelithiasis, from the gall bladder, and so on, inasmuch as from a roentgenological point of view the appearances are frequently identical. In 9 per cent of the cases in our series the diagnosis was rendered doubtful by the presence of adhesions.

As we have frequently pointed out, unless due care be exercised one may be misled by certain reflex or spastic conditions of the stomach. It is not uncommon to observe a stomach presenting a persistent filling defect in a definite area and continuing over a period of an hour or two. In one instance under observation it persisted over a period of forty-eight hours. In this particular case the filling defect was so large and so definite, notwithstanding the fact that the clinical evidence was negative, that the case was used for repeated demonstrations of the typical ulcer. Operation, however, revealed a perfectly normal stomach. In such cases the spasm of the stomach can easily be eliminated by the administration of full doses of atropin for one or two days until the patient is well under its influence. A second examination made under these con-

ditions will generally show that the suspicious area has completely vanished, and that the defect was in reality a spasm.

When ulcerations are situated at or near the pylorus, important aid is rendered in diagnosis by the presence of obstructive signs produced by the cicatrix while the ulcer is healing. These signs are not only revealed by the *x*-ray examination, but also by clinical methods. It occasionally happens, however, even though the clinical history as well as the retention meals point definitely to obstruction, that this condition may be overlooked by the roentgen-ray examination.

In a patient, Mrs. C., in whom the clinical signs and retention tests pointed definitely to obstruction, the *x*-ray gave no evidence of this condition. Levy, too, has recently pointed out that the roentgen ray as commonly employed is at times not as delicate in determining gastric motility as the usual retention meals. On the other hand, there are many instances of partial obstructions in the early stages of gastrectasia where the obstruction is still incomplete in which the diagnosis is often very difficult. The clinical signs of this condition appear so intermittently that they are overlooked, while on the other hand this condition can be definitely determined by *x*-ray examination.

Carcinoma of the Stomach. The roentgen-ray diagnosis of carcinoma of the stomach is not always positive, especially in the early stages, as the lesion may be mistaken for simple ulceration.

In cancer of the cardiac area the stricture and filling defect may be absent in early lesions, and the condition may be overlooked on account of the great difficulty in properly filling the cardiac end of the stomach.

In lesions in the body of the stomach one may have an extensive growth, and yet the patient may complain of very few symptoms, inasmuch as the motor activity is not interfered with. As this lesion does not affect the cardiac or the pyloric orifice, obstructive symptoms are absent, the stomach emptying at the normal rate or perhaps a little more rapidly than normally. The roentgen-ray examination of the stomach of this form generally shows that the peristaltic waves are interrupted in their course at the seat of the lesion, inasmuch as the lesion itself is hard and indurated, and does not admit of further peristaltic movements. In addition a persistent

filling defect is almost always present. In the third class of cases, that is, in lesions about the pylorus, the symptoms arise early, as a rule, and are due to a partial obstruction, to which attention has already been called.

From a roentgenological point of view we classify growths at the pylorus into two forms.

The first, the annular carcinoma, has its origin within the pylorus itself, and although it may be very small in size, produces symptoms relatively early, as it soon causes a greater or less degree of obstruction.

The second type also has its origin at the pylorus; it is not annular in form, but invasive, most frequently extending along the wall of the stomach, especially at the pylorus. Such a growth may, or may not, produce early obstruction.

The annular type of carcinoma is easily recognized, inasmuch as the stomach is observed to be perfectly normal except at the pyloric end. The pylorus, instead of being clear-cut and sharp, is generally somewhat thickened and slightly depressed in the center, so that the structure assumes the shape of a crater.

The second type of carcinoma may exist for some time without being recognized, because in the absence of any symptoms of obstruction the patient, being still in a comfortable state, does not present himself for an examination. In this type of growth one finds a persistent filling defect in or close to the pylorus, and ascending away from it. The mass is indurated and free from peristaltic waves.

Notwithstanding the very definite *x*-ray signs of gastric carcinoma, there are instances, especially in the early stages, when this condition is not recognized. This is due to the fact that the defect is so small as to be entirely overlooked, and the functional activity of the stomach is not interfered with.

On the other hand unless due care be exercised spastic or reflex conditions may lead to errors in diagnosis. It is not uncommon to observe a large, persistent filling defect in a definite area simulating carcinoma and continuing over a period of hours. In one case this defect persisted constantly without intermission for ten days, and was only found to be a spasm at operation. In a second instance the roentgenological examination was made by one of our well-

known roentgenologists with a diagnosis of carcinoma. Three months later the patient was seen by us, and the roentgenological examination showed identically the same condition as was present at first. The patient was given atropin in full doses, and when the second examination was made the filling defect had completely disappeared. The patient, however, not being content, insisted upon an exploratory operation, which revealed a perfectly normal stomach.

In the *x*-ray study of gastric carcinoma the differential diagnosis between this condition and ulcer is often very difficult. It is still a much-debated question as to whether carcinoma of the stomach has its origin primarily as such, or is the result of a transition from an old ulcer. If the latter view be correct, one can readily understand the difficulty in determining when the transition into malignancy begins. The situation of both carcinoma and ulcer is very frequently the same, although we observe carcinoma more frequently on the greater curvature than ulcer.

In the differential diagnosis between the two conditions the points to be taken into consideration are as follows:

1. *Peristalsis.* In carcinoma, unless there is obstruction there is always hypermotility with rapid evacuation of contents. In ulcer there is always hypermotiltly, with a spasm of the pylorus and more or less retention of contents.

2. *Position.* Carcinoma may occur in any part of the stomach. The invasive lesions are more frequently seen on the lesser curvature near the pylorus, and less frequently on the greater curvature. The massive growths are more generally seen on the greater curvature, whereas ulcer is generally observed on the lesser curvature near the pylorus, although it may occur on the greater curvature.

3. *Filling Defect.* In carcinoma the filling defect is generally surrounded by an invasive area, which, while not appearing on the plate, interferes with motility, producing an apparently large dead area. In ulcer the filling defect is much smaller, and is not so apt to have the immediate peristaltic waves interfered with, although if the inflammatory area be large there may be also a dead area surrounding the filling defect.

Carcinoma of the pylorus in the earliest stage is generally annular and produces a crater-like appearance. In ulcer of the

pylorus there is a filling defect, but it does not generally assume the crater-like appearance. When any of these conditions pass on to the obstructive stage the change that is caused by the dilatation may mask the signs associated with the filling defect.

In our experience in the very early stages of gastric cancer it is frequently impossible to determine whether we are dealing with a malignant or a simple ulceration. Our main aim, however, is to decide whether the lesion at hand is really an ulcer or not. Inasmuch as indurated gastric ulcers have at times a tendency to become malignant and produce roentgenograms similar to those which are cancerous, they must be included in the same class. The exact diagnosis must be cleared up by further investigation into the clinical history and the examination. But even under these conditions there are many instances in which the diagnosis may still remain in doubt until operation and microscopic examination of the specimen after removal finally establish the true nature of the disease.

Gall-bladder Disease and Gall Stones. The roentgen-ray indications of gall-bladder infections are revealed by the presence of adhesions dragging the stomach and duodenum over into the direction of the gall bladder. The adhesions, however, need not necessarily extend from the stomach and duodenum, but may arise directly from the gall bladder itself, extending to various parts of the intestinal tract, and are apt to produce varying degrees of stasis, retention, and obstruction according to their extent, and thus give us a definite picture in the plates as to the chronicity of the gall-bladder disturbance. Frequently this condition is associated with a filling defect in the duodenum, and a deformity of the duodenal cap. When that condition arises it is frequently impossible to determine whether we are dealing with a primary gall bladder or duodenal disease, and it is only possible by a study of the clinical history, as we have already pointed out, that a correct diagnosis can be made.

The demonstration of gall stones by the roentgen rays has itself reached a position that warrants its more general use as an aid in diagnosis, and if the gall-bladder region is examined for stones prior to the bismuth examination of the gastro-intestinal tract, gall stones may be absolutely demonstrated, in a certain percentage

of the cases, depending largely upon the amount of calcium salts present. Gall stones composed entirely of pure cholesterin are practically invisible to the ray. It is difficult to give percentages, as they vary so markedly according to the type of case and the operator that figures would be misleading. One must remember, however, that a negative diagnosis does not rule out gall stones.

The calcium mixture is the only part shown by the *x*-ray, and the clearness of the gall stones upon the plates will be proportionate to the amount of calcium. Inasmuch as in a large proportion of patients affected with gall stones for some time, the stones contain calcium, it is more than likely that, as the technic becomes more perfected, gall stones may be demonstrated in many instances, especially where the symptoms have been of long duration.

There are sources of error here too, however, the main ones being renal calculi, calcified mesenteric glands, and costochondral ossifications. There have been a number of instances in our experience in which shadows were diagnosed as gall stones which were not found present at operation.

Chronic Appendicitis. The roentgen-ray examination of the appendix itself in its chronic state is capable of rendering valuable service in a certain number of instances. When the lumen of the appendix is closed as the result of an obliterative process, bismuth will fail to enter.

We have frequently pointed out how partial obstructions of the pylorus are apt to lead to the production of adhesions extending to the lower right quadrant, dragging the stomach in that direction, and these are often associated with chronic disease of the appendix. Adhesions associated with the appendix, however, need not extend from the stomach or even from the duodenum, but may arise from the appendix itself or its surrounding structures and may lead to a varying degree of cecal or ileal stasis or even to partial colonic obstruction.

With proper technic the appendix may be visualized in many instances, whereupon roentgenographs of this organ may be made.

Case recommends a special technic for the examination of the appendix:

"1. The necessity of examining the patient in the horizontal position with the screen held over the abdomen, and the tube underneath the table.

2. The necessity of palpating the abdomen under the screen, with the gloved hand or preferably with the wooden spoon, and noting the localized tenderness. The time of the examination is of some importance. Shortly after the cecum begins to fill the appendix also fills. This usually occurs in six hours, although there are many cases in which the cecum is filled earlier or later. From this time on until the bowel is empty, and frequently for some time afterward, the appendix remains visible.

"The ordinary technic of roentgenology with the patient standing or lying is not likely to show the appendix; we must first find the appendix fluoroscopically, and then make the roentgenograph. When the appendix remains visible for more than a day or two after the bismuth examination, it is, in proportion to its poor drainage, a dangerous appendix."

There are certain instances in which the bismuth shadows persist for many hours or days, and sometimes weeks after the bowel has been emptied of its bismuth.

While the *x*-ray renders valuable service in diagnosis, in many instances of chronic appendicitis there are a certain number in which it does not demonstrate this condition, or where its results may even be misleading. This may be due to the fact that on account of its unusual position the appendix cannot be visualized, or, as has already been pointed out, that its lumen is closed, due to an obstructive process, so that the bismuth is prevented from entering, or finally to the presence of mild adhesions which may not be revealed in the plates.

Attention must also be called to a potent source of error which should always be borne in mind. As a reflex condition a chronic appendicitis may give rise to a picture somewhat similar to that observed in duodenal ulcer—that is, there is a gastric and duodenal hypermotility with a definite filling defect, and deformity of the duodenal cap—if this picture is rather marked and the appendiceal adhesions are slight, one can readily understand how a chronic appendicitis might be mistaken for a duodenal ulcer, and in fact this error is sometimes made. In instances of this kind the plates must be most carefully studied, repeated examinations made if necessary, and in most instances a combined fluoroscopic examination, study of the plates, together with the clinical history, will point to the correct diagnosis; but even at times after a most careful investigation in every direction, the correct diagnosis may still remain in doubt.

Intestinal Adhesions and Angulations. When the bismuth meal is taken it ordinarily reaches the cecum in from seven to ten hours, the transverse colon in twelve, and the sigmoid and rectum in eighteen to twenty hours. Delay in the passage of the bismuth may be due to the various conditions—to a dilatation and retention in the cecum; to ptosis of any portion of the colon, especially the transverse colon with intestinal stasis; to adhesions in various portions of the intestinal tract, including the gall-bladder region, cecal region, splenic flexure or sigmoid, or to a redundant transverse colon or sigmoid; to ileal stasis or frequently to angulations at the hepatic or splenic flexures, and finally to carcinoma of the colon. Carcinoma of the colon may exist for a long period of time before obstructive symptoms are noted. Filling defects are frequently observed in this condition, but great care must be exercised to be positive of the constancy of these findings, both by fluoroscopic examinations and by means of bismuth enemata.

In a special instance which has come to our attention in which a capable roentgenologist made a diagnosis of carcinoma of the ascending colon, and in which the diagnosis was confirmed by all the methods usually practiced by roentgenologists, the filling defect and partial obstruction was found due to the dragging down of the bowel by adhesions connected with an inguinal hernia. Inasmuch as adhesions are detected only by changes and delays in motility, great care must be exercised in drawing conclusions regarding these findings.

Spasmodic contractions can usually be eliminated by the free administration of atropine or belladonna, and in doubtful cases repeated examinations must be made. There can be no question that frequent errors are made in the diagnosis of intestinal adhesions, which are usually due, however, to a lack of proper technic or insufficient observation.

We have attempted in a rather imperfect way to direct attention to the fact that as yet the results of roentgenological diagnosis are not sufficiently perfected in all cases to be relied upon alone. While the *x*-ray is probably our one greatest aid in diagnosis, yet it is only one method of examination, and the best results are obtained by combining its use with a thorough clinical study.

A FEW UNUSUAL COMPLICATIONS AND SEQUELÆ OF INFLUENZA

By Channing Frothingham, M.D., Boston, Mass.

In using the word influenza in the title of this paper, it is appreciated that considerable doubt exists in the minds of some workers on this subject as to the relation of the Bacillus of Pfeiffer to the acute infectious disease called influenza. There is no doubt of the presence of the influenza bacillus in a certain number of the cases. It may, however, be a secondary invader just as the pneumococcus, streptococcus, and other organisms are; and the agent which causes the symptom complex known as influenza may be due to some as yet undiscovered virus.

It seems fair to assume, however, that the recent epidemic which has swept through the United States and has been so prevalent in the army camps is the same disease as has been described in the text books of medicine under the title of Influenza, whatever may be its cause.

As the disease occurred at Camp Devens, Mass., it presented the following typical course: sudden onset with or without chill, fever, headache, aching and pains, especially in the back and extremities, congestion of the conjunctiva, and involvement of the mucous membrane of some part of the respiratory tract. In a few days, if no complications occurred, the temperature returned to normal and the patient was left considerably more prostrated than one would suppose from so short an infection. In a large percentage of the cases, after two to four days, the temperature, instead of continuing to drop to normal, would rise again. It was felt that this secondary rise was due in most cases to an extension of the inflammatory process from the bronchi into the surrounding lung tissue, whether or no evidence of a broncho-pneumonia could be found. In most of these cases with a secondary rise in temperature, evidence of pulmonary involvement appeared, either as dullness on

percussion, diminished breath sounds, localized fine crackling râles, or even signs of definite consolidation. After this secondary rise, the temperature would remain elevated for several more days and either a fatal termination would occur, the temperature would drop by lysis, or the fever would end abruptly by crisis. The duration of the fever following the lung involvement was quite variable and in some cases the signs of definite consolidation in the lung would appear only after the temperature had returned to normal.

The involvement of the lung tissue in these cases has been studied carefully by Wolbach, who describes quite typical lesions for the various types of organisms which invade the lung. The principal organisms causing the different types of pneumonia are the influenza bacillus, the pneumococcus, and the streptococcus. One or more may be present in the same case. From the clinical signs, it is usually not possible to tell what type of invading organism or lesion is present in the lung tissue. The clinical course of this disease as met with at Camp Devens will be described in detail by Fulton, who has made a careful clinical study of these cases. Therefore, in this study, attention will simply be called to certain of the complications of this disease which seemed to be rather unusual or of special interest.

Lord, in Osler's "System of Medicine," mentions a variety of complications and sequelæ that may follow influenza. Of them, undoubtedly some are due to the secondary invading organisms as well as to the virus which causes the original disease. He mentions, as quite common, involvement of the various sinuses and cavities connected anatomically with the respiratory tract. Following lung involvement, he speaks of breaking down of lung tissue in some cases with abscess formation which occasionally ruptures into the pleural cavity, causing empyema and pneumothorax. These pulmonary involvements are usually associated with mixed infections. The development of a chronic bronchitis with bronchiectasis is not uncommon. Apart from the respiratory tract, Lord mentions cases in which influenza bacilli were obtained in pure culture from an inflamed gall bladder, from a phlegmon of the arm, and from an inflamed periosteum. On the part of the central nervous system he mentions various psychoses, myelitis, paralysis of various nerves, and a peripheral neuritis.

In addition to these unusual complications, Elsner, in "Monographic Medicine," mentions a case of malignant endocarditis, caused by the influenza bacillus, and calls attention to the possibility of hemorrhagic diathesis following the disease. W. H. Smith, in "Forchheimer's Therapeutics," mentions thrombosis and phlebitis as among the rarer complications.

Among the influenza cases at Camp Devens, involvement of the accessory sinuses and the middle ear occurred not infrequently. From some of these cases, Wolbach recovered the influenza bacillus in pure culture at autopsy. A peculiar feature in some of the cases of otitis media was the absence of pain associated with the infection. Often the first indication the patient had of any trouble with the ear was the appearance of a purulent discharge.

The chief pulmonary complications met with at Camp Devens were the various types of broncho-pneumonia and lobar pneumonia which will be described clinically by Fulton and pathologically by Wolbach. Bronchiectasis was also a common finding in the autopsy room, and, as it will be covered by the reports of these workers, it need only be mentioned in this study.

A much more unusual complication associated with the lung involvement was the escape of air from the respiratory tract into the interstitial tissue of the lung, and its extension from there along the interlobular septa of the lung out through the root of the lung, through the mediastinum, and into the subcutaneous tissues of the neck just above the clavicles. From this point in some cases it extended throughout the subcutaneous tissues of the entire trunk and extremities, and up on to the face.

Usually the first indication of this escape of air was the appearance of crepitation of the skin in the neck just above the clavicles on one side or the other. In some instances this was preceded by substernal pain, and pain referred to the abdomen. It is assumed that this discomfort was produced by the tension created by the air working its way through the mediastinum. As a rule this pain subsided when the air appeared in the subcutaneous tissues above the clavicles. This subcutaneous emphysema usually appeared from the fifth to the tenth day of the disease, and the prognosis in these cases was usually bad. In a few cases, however, the subcutaneous emphysema gradually disappeared, the lung signs began to clear,

the temperature subsided, and the patients made a complete recovery.

Just at what point the air escapes from the respiratory tract is not clear, but it seems probable that it is in the neighborhood of the lesions in the walls of the bronchioles and alveolar spaces which Wolbach describes as peculiar to the influenza organism. It is surprising that the air should force its way from the point of escape through the subcutaneous tissue as far in some instances as the ankle, rather than return through the air passages. It suggests some valvular action at the point of escape which prevents the air from returning to the air passage after it has once leaked out.

Summary of a Case Showing Subcutaneous Emphysema. F. H., Base Hospital, Camp Devens, Register No. 39131, thirty years old, past and family history as recorded unimportant. He entered the hospital, September 21, 1918, having been ill with influenza for six days. On entrance, a diagnosis of broncho-pneumonia was made. A type four pneumococcus was reported in the sputum. On September 25th he complained of abdominal discomfort with tenderness at McBurney's point. On September 27th subcutaneous crepitation appeared in the neck. By September 28th the air had extended over the front of the trunk to Poupart's ligament on the left and below it on the right. The temperature gradually returned to normal and remained so after the 15th of October. The air in the subcutaneous tissue gradually disappeared, so that it was gone by October 20, 1918. The evidence of pulmonary infiltration slowly cleared up, and after a prolonged stay in the hospital he was discharged well on December 27, 1918.

Although the air bubbles were found in the interstitial tissue of the lungs, quite close to the pleural surface, they did not, as a rule, break through the pleura into the pleural cavity. In two cases, however, the air did leak out into the pleural cavity, causing in one a double pneumothorax, and, in the other, a unilateral pyopneumothorax. In both these cases, this complication occurred late in the disease after the acute stage of the pneumonia was over and convalescence apparently well started. In both cases, the air in the pleural cavity was under pressure, so that it whistled through the needle upon puncture, thus suggesting the same valvular effect mentioned above, and a gradual blowing up of the pleural cavity with air.

Summary of the Case of Double Pneumothorax. J. S., Base Hospital, Camp Devens, Register No. 23285, twenty-five years. As recorded, family and past history have no bearing on present condition. He entered hospital on September 15, 1918, having been ill for three days with symptoms of

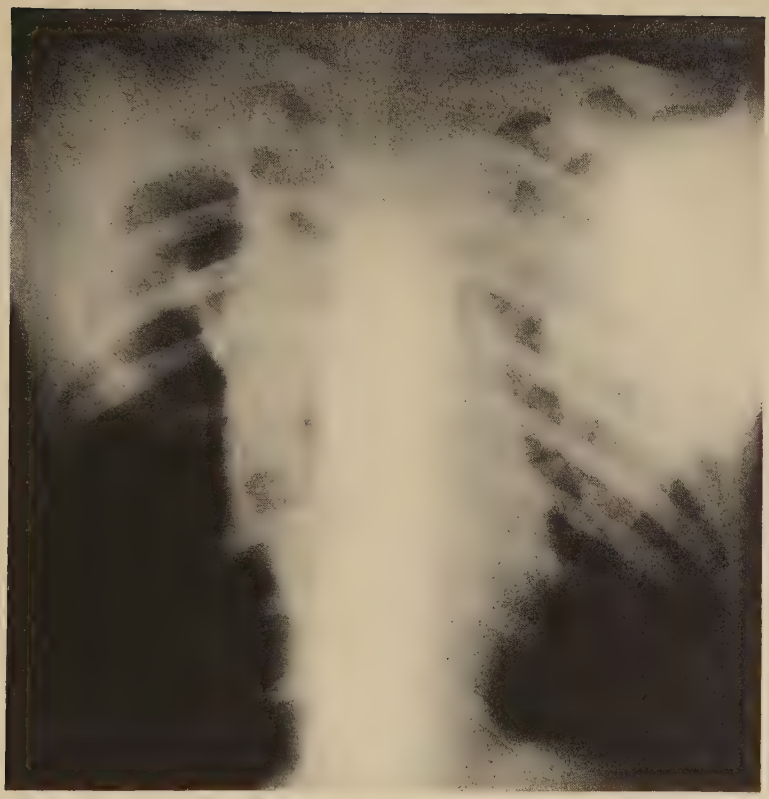

FIG. 1. ROENTGENOGRAM OF CHEST OF PATIENT WITH DOUBLE PNEUMOTHORAX.

It Shows almost Complete Collapse of the Left Lung, Displacement of the Heart to the Right, and Partial Collapse of the Right Lung.

influenza. From entrance to October 8th temperature remained elevated, due, apparently, to a broncho-pneumonia. From October 9th to October 22d temperature, pulse, and respiration normal. Lung examination during this period still showed râles in both sides, and at the right apex bronchial breathing. From October 23d to death the temperature occasionally went up to 100°. On the 24th he complained of abdominal discomfort and vomited. His abdomen suggested acute appendicitis. The leucocyte count showed 23,000 with 68 per cent polynuclear leucocytes. The pulse and respiration became more rapid and the patient became gradually more cyanotic from October 25th to 31st. On October 31st examination revealed a double pneumothorax in which the left lung was quite markedly collapsed, being held out by a few adhesions towards the apex, and the right lung not so completely collapsed, because the adhesions were more generally scattered. (See Fig. 1.) As the patient was apparently dying from the mechanical interference with respiration, the air was withdrawn from the left pleural cavity to allow the lung to expand. Although it expanded, it collapsed again in a few moments, as the air apparently leaked into the pleural cavity quite rapidly, and the patient died shortly afterwards. At the autopsy, No. 242, Base Hospital, Camp Devens, the peritoneal and pericardial cavities were normal and the interest centered entirely in the lungs and pleural cavities. There was some air in the anterior mediastinal tissues. The pleural cavities showed both fibrous and fibrinous adhesions especially pronounced towards the apices. The right pleural cavity was more extensively obliterated than the left. There was no free fluid in either and both lungs collapsed insofar as the adhesions permitted. On section, both lungs showed marked bronchiectatic cavities in the upper lobes and evidence of peribronchial inflammation. These lesions extended to and involved the pleura near the apices, and the air leaked through these lesions into the pleural cavities.

A less spectacular but important sequela of influenza as regards treatment and prognosis is the late involvement of the pleural cavity with an inflammatory process. Usually two or three weeks after the beginning of the pneumonia, signs suggesting a pleural effusion would develop, and on tapping pus would frequently be found. In many of these cases, subsequent tapping just prior to operation, and even operation itself failed to locate any pus. At autopsy the reason became evident, for instead of free pus in the pleural cavity, or one large walled-off pocket of pus, the pleural space would be obliterated with adhesions varying from fresh fibrinous to dense fibrous ones, and scattered through these areas were pockets containing from a

few drops to sometimes 20 or 30 c.c. of pus. Furthermore, the line of demarcation between lung and pleura was frequently difficult to make out, and it was felt that some of these pockets of pus were actually in the lung itself and represented small lung abscesses. The *x*-ray examination was not of special value in differentiating between this process in the pleura and a collection of fluid which could be successfully treated by operation. The character of the inflammatory lesion made it impossible to treat the condition by drainage, and the presence of this inflammation remained a constant source of danger to the patient. For, in two instances, the organisms finally passed into the circulation and then produced a general peritonitis. In several others the inflammation extended to the pericardial cavity and produced suppurative pericarditis. The prognosis in these cases, therefore, must be most guarded. As attempts at drainage by operation or frequent tappings are so unsatisfactory, it is difficult to decide what is the best procedure for treatment. The pus from these tappings showed no one organism constantly. In some cases the influenza bacillus was recovered, but always associated with a pneumococcus or streptococcus. In other cases, one of the latter two were found alone.

Summary of a Case of Suppurative Pleurisy. R. H., Base Hospital, Camp Devens, Register No. 28691, twenty-six years, colored. He entered the hospital on September 20, 1918, having been sick for one day with the usual signs of a broncho-pneumonia. For the next six days he ran a severe course, temperature ranging from 101° to 104.6°, with the chest signs increasing until patches of more general consolidation appeared. The temperature became somewhat lower after October 2d, until the patient's death November 15th, varying from normal or below to 102°, but the chest signs did not clear up, and the pulse remained elevated. About October 14th the chest signs changed so that fluid was suggested on the left side, both by physical examination and *x*-ray, and on puncture of the left pleural cavity on October 26th, a small amount of pus was found. Subsequent puncture on the surgical service in the next interspace failed to find pus and the chest was not opened.

At autopsy, No. 246, Base Hospital, Camp Devens, the pericardial and peritoneal cavities were normal. The aortic valve showed some acute vegetations, but the main interest centered upon the condition in the pleural cavities and lungs. The right pleural cavity was free from fluid or adhesions. The right lung showed a broncho-pneumonia and peri-

bronchial infiltration. The left pleural cavity was practically obliterated, anteriorly and around the apex by fibrinous and rather easily separated adhesions. In the axillary region the adhesions were more tough and did not separate easily, so that visceral and parietal pleura came off together. On breaking through this tissue, in one or two places, small collections of pus were met. At one point, at the junction of the lower and upper lobes, on the left, just beneath the pleura, a small area of necrotic tissue in the lung itself was present. Between the two lobes was a gelatinous exudate, forming a septum about 1 to 2 centimeters in thickness. The lung showed some areas of consolidation and the bronchi were prominent, suggesting infiltration about them. The other organs showed nothing of interest.

Although the chest complications which appeared at Camp Devens furnished the most interesting study, there were a few other unusual sequelæ that were of interest. Several instances supported the view that the barriers against invasion of other organisms are broken down to some extent by this disease. The frequent invasion of the lungs with the pneumococcus and streptococcus is the most striking example of this. Another example was furnished by the occurrence of a sudden flare up in the number of cases of meningococcus meningitis in the hospital among the convalescent influenza cases. From their distribution in the hospital it was pretty clearly demonstrated that the cases were not infected from each other, and it was felt that they were probably chronic carriers in whom the organisms succeeded in invading after the resistance had been lowered by the influenza. It is interesting to note that following the installation of a drop of argyrol in each nostril of all the patients, three times a day, the appearance of new cases practically ceased.

Another instance of lowered resistance was furnished by a group of cases of abscesses, usually single and apparently caused by a blood-borne infection. These abscesses occurred in a variety of places, among others, about the shoulder, in the popliteal space, and in the rectus muscle. In each case, the evidence pointed to the causative agent arriving through the blood stream, as there was no superficial lesion which could be considered as a point of entry.

Summary of a Case of Influenza Complicated by Abscess. W. S., Base Hospital, Camp Devens, Register No. 25010, twenty-one years. Entered hospital September 16, 1918, having been sick for three days. He presented

the usual typical picture of influenza with bilateral broncho-pneumonia. He ran the usual course with fever ranging from 101.5° to 105.2° until it came to normal in the morning of October 2d, but remained elevated in the afternoons for a few days longer. On September 25th a purulent discharge appeared from the right ear. From October 3d to 16th, although the temperature was only slightly elevated, he was mentally dull and at times delirious. On October 18th, he complained of abdominal pain during the night and inability to pass water. Upon catheterization, only 60 c.c. of clear urine were obtained. A circumscribed tumor was found just above the pubis, about the size of a baseball, which was tender and reddened. During the next two days the tumor increased in size and tissues became somewhat edematous. On October 20th the tumor was opened and an abscess drained. This abscess was in the rectus muscle sheath and showed a pneumococcus in the culture. The abscess gradually cleared up, the patient's general condition improved, and he was discharged well on January 17, 1919.

Another interesting group of complications observed in this epidemic were those referable to the nervous system. At Camp Devens these conditions were more rare than the chest complications. Whether they were due to the causative agent of the disease, whatever it be, or to the secondary invaders is not definitely established. Several cases showed a toxic psychosis during or just following the height of their infection. In several others it was felt that permanent insanity such as dementia precox, or constitutional psychopathic state, or manic depressive insanity, which would have eventually developed, was hastened by the infection.

Summary of a Case of Toxic Psychoses. W. B., Base Hospital, Camp Devens, Register No. 25069, twenty-five years. Entered the hospital on September 16, 1918, with a diagnosis of influenza. His past history and family history as recorded were negative. On September 22d the diagnosis of pneumonia was made. On October 5th mental symptoms began to appear. He became confused, difficult to handle, and inclined to wander off. He remained in this confused state until November 6th, when he suddenly came back to normal condition. He was discharged to duty on November 18, 1918, well.

Another more serious complication was that of a transverse myelitis of the spinal cord. In two cases, the symptoms were pronounced, and in one nurse, a transitory incontinence of feces and

urine for one day was looked upon as a mild form of the same condition.

Summary of a Case of Transverse Myelitis. S. B., Base Hospital, Camp Devens, Register No. 36919, twenty-six years. Entered hospital September 26, 1918. Past and family history were unimportant as recorded. He had had an attack of influenza the week preceding entrance, but had been treated outside the hospital. Following this he had not passed urine for two days and was unable to stand up unassisted. A note on September 28th showed retention of urine, incontinence of his bowels, paralysis of both legs, and disturbance in sensation of both legs. A diagnosis of transverse myelitis was made by the neurologist. His paralysis slowly improved and on January 6th he was discharged to duty practically well.

Neuritis involving one or more nerves was one of the distressing complications of the influenza. Persistent pain in the sciatic nerve was observed and in another case a more general distribution involving the left arm and leg.

Summary of Case of Multiple Neuritis. S. B., Base Hospital, Camp Devens, Register No. 28512, twenty-two years. He entered the hospital on September 20th with diagnosis of influenza which began the day before. The past and family history as recorded were unimportant. On September 28th a broncho-pneumonia developed and on October 3d he was jaundiced. On October 8th pain began in his left arm, side, and leg, which was diagnosed by the neurologist as a multiple neuritis. Following this a bedsore developed and signs of general sepsis began to appear. He eventually succumbed on December 25, 1918, after a long-drawn-out septic infection.

In presenting these cases, the object has been to remind the profession of some of the unusual complications which may follow influenza, and to call attention to the reduction in the resistance against other organisms that this disease seems to produce. Of the many complications which this epidemic presented at Camp Devens the escape of air into the subcutaneous tissue or pleural cavity and the various pleural inflammations were perhaps the most interesting.

LINKS OF ELECTRICITY IN THE HUMAN SYSTEM

By Sir James Grant, K.C.M.G., F.R.C.P. (Lond.),
President and Chief of Staff, General Hospital, Ottawa, Canada

FEW subjects are attracting greater attention at present than electricity and the relief it affords in diversified abnormal conditions of functional nervous activity. Its precise action as a remedial agent is still surrounded by doubt and uncertainty. As to what electricity actually is no satisfactory answer has as yet been given. Lord Kelvin himself once told me that he did not know.

Great strides are being made in many lines of electrical and mechanical industries, but we are only at the beginning of our discoveries of methods for the promotion of health and longevity by the action of this mysterious agent, and a greater degree of interest is manifest in this subject than at any period in the present century. Colleges and hospitals are establishing special departments of electricity, and the prospect that its practical application in medical science will prove of undoubted value is brightening rapidly. Dr. Tait McKenzie, of Philadelphia, has informed me that when in charge of a disabled section of the army, in the neighbourhood of London, he found electricity of vast service in his efforts to restore functional troubles, chiefly of the muscular system.

One of my first professional efforts was to conceive the idea that lumbago might prove a form of abnormal electrical storage in the human system, and be discharged by punctures of needles as rapidly as the Leyden jar is relieved of its electrical contents, by a touch of the finger.

My first case, over forty years ago, was a source of surprise and pleasure, through the suddenness of relief from all pain, and return of complete functional activity, by the insertion of No. 8 fine needles into the tense lumbar muscles. One of the most remarkable cases of electrical treatment came to light during a visit to Scotland in 1902. I had been invited to Skibo Castle, and on arriving there, learned of the sudden

illness from lumbago of a great magnate. I was asked to see him. He was confined to his bed, unable to move or help himself in the slightest degree, every effort being followed by intense pain and suffering. The lumbar region was freely exposed, the muscles of which were firm as a board on pressure with no evidence of increased temperature. The attack was sudden, during the night, without any assignable cause. In treating him, the back was sponged with warm water and dried carefully. The tense muscles on either side of the spine were punctured by needles, eight or ten in number, on either side, inserted about an inch apart for half their length, by pressure of the thumb nail. This was somewhat difficult, owing to the extreme tension of the muscular tissue. After ten minutes every needle was removed, with resulting ease and comfort, owing to the almost immediate relaxation of the entire lumbar muscles. In half an hour he arose and walked around the room, amazed at the sudden transition from intense suffering to complete relief. In an hour he dressed, walked to his drawing room perfectly recovered, and from that time to the present has enjoyed perfect freedom from lumbago.

In the years that have passed the results in all such cases have proved equally satisfactory.

Nerve block in any form interrupts functional activity of affected parts, and its treatment is a serious problem. Sherrington of Cambridge and Macdonald of Sheffield first found that salts of sodium and potassium were chief constituents of the axis cylinder of nerve tissue. In cases of brain overstrain, I have observed sections of the limbs that were completely defective in sensation when tested by electricity. After sponging the skin with water and applying electricity eight or ten minutes, sensation was aroused to a high degree of intensity. This temporary arrest of feeling and sudden return suggests the idea of a block in the axis cylinders, in which a solution of continuity must have taken place, and prevented transmission of the electric current. An interesting problem thus arises: What caused the interrupted transit of the current? The most probable theory is that poisonous gases in the alimentary canal, the outcome of imperfect assimilation of food products, produced a chemical change in the saline constituents of the axis cylinder, which is overcome by the persistent transference of the electric current. The chief cause of nerve block is in the abdominal cavity, and is due to imperfect assimilation of food products, thus bringing about a degree of lowered vitality and general functional inactivity

in the whole digestive process. A current through the extremities, passing along the filaments of the sciatic and saphenous nerves, is twofold in character. First, it removes the nerve block in the nerve tissue, and establishes the action of the nervous system, so closely associated with the abdominal ganglia.

More deaths result from excessive amounts of food than from alcohol. The most fatal period is from the fiftieth to the sixty-fifth year. At this period imperfect assimilation of food products and a tissue destruction of such organs as the kidney and liver occurs. Such conditions are observed to begin chiefly about the forty-fifth year, at which stage of intestinal activity marked relief will be derived from electric abdominal massage, ten minutes once daily, two hours before or after meals.

For many years I have adopted this method of increasing the assimilation and lessening the formation of poisonous gases in the alimentary canal, with the most practical and gratifying results. The day is not far distant when electric abdominal massage will assist the entire domain of therapeutics by counteracting the influence of alimentary poisonous gases, lessening the therapeutic activity of remedies absorbed and circulated by the lacteals and lymphatics for relief from disease. This treatment, carried out systematically, has been successful in extending in comfort many a life to the eightieth and eighty-fifth year.

THE AGE INCIDENCE OF THE SCAPHOID TYPE OF SCAPULA

ITS BEARING UPON PROBLEMS OF RACIAL MORBIDITY

By William Washington Graves, M.D., St. Louis, Mo.

"The proper study of mankind is man."—Pope.

In 1910 I described a very frequent variation of the human shoulder-blade, which I believed to be an anomaly in development of hereditary, clinical, and anatomical significance (1). This type of scapula was designated "scaphoid" for the reason that its most striking characteristic is a concavity (Fig. 1, *C*) of the vertebral border below the scapular spine as opposed to convexity (Fig. 1, *A*) of this part of the bone, which before that time had been and still is considered a characteristic of the "normal" human shoulder-blade.

A study of dry bones soon disclosed the fact that those whose vertebral borders were straight (Fig. 1, *B*) had several of the characteristics found in those having marked concavity of the vertebral border below the scapular spine. Moreover, individuals in whom this part of the bone was found to be straight disclosed general characteristics similar to, although, as a rule, less marked than, those in whom it was concave. I have, therefore, called all scapulæ the scaphoid type whose borders in this part of the bone were straight, slightly, or definitely concave. This type of scapula was found to differ from the type heretofore described as normal in five or more anatomical particulars.

Studies of embryo and fetal forms disclosed the same types of scapulæ as are found in all the later periods of development. (Fig. 2.) Studies of whole families, through several generations, showed that in most instances the scaphoid type of scapula was distinctly hereditary, but that under certain conditions parents having normal scapulæ begot progeny having the scaphoid type. Finding this type of scapula in embryo forms and in all subsequent periods of

development, and finding that it was transmitted from parent to child and so on through several generations, I was led to conclusions that nothing in the life of the individual after his birth could cause him to have a normal scapula if at birth it was scaphoid, nor a scaphoid scapula if at birth it was normal. Notwithstanding the seeming convincing evidence upon which these conclusions were founded, nothing short of observations on a number of individuals during periods of growth, extending over a number of years, could supply the final proof of the unchangeableness in the essential form of scapulæ, independent of disease processes after birth. I have made observations extending over a period of twelve years on a number of individuals in various periods of development, with the result that their scapulæ have shown no change: those which were scaphoid and those which were normal are to-day as they were in the beginning.

Studies in comparative anatomy and studies of man point to the conclusion that the type of scapula described by anatomists as normal best fulfills the scapular requirements of man. Moreover, the study of living human beings readily demonstrates the fact that the type of scapula described by anatomists as normal is the type usually found in the better types of man—in those possessing to a good degree symmetry, proportion, harmony, and adaptation of their structures and functions. While we are able to recognize a normal type in reference to a bone, we meet with difficulties when we attempt to apply this term as a standard to the whole individual. For many reasons we seem unable to define the normal, but we can recognize the *attributes* of the ideal in total human development, even though we are unable to standardize this ideal. The chief attributes of this ideal seem to be symmetry, proportion, harmony, and adaptation of structures and functions—the same in human beings as in all living things. Now, a consideration of these attributes when applied to a study of the whole individual will usually enable us to discern his *nearness to*, or his *remoteness from*, this ideal in human development. The individual possessing to a good degree the attributes of this ideal usually discloses "the healthy mind in the healthy body," and he is quickly recognized as belonging to the better types of the race. As physicians we seldom come in contact with these types in a professional way—with the near-to-the-ideal in de-

FIG. 1. *A*: "NORMAL" TYPE; *B* AND *C*: "SCAPHOID" TYPES.

FIG. 2. EMBRYOS IN APPROXIMATELY THIRTEENTH WEEK. THE UPPER FIGURE SHOWS THE "NORMAL" AND THE LOWER A "SCAPHOID" TYPE OF SCAPULA.

velopment—because the symmetry, the proportion, the harmony, and adaptation of their structures and functions seem to supply them with those peculiar qualities which enable them to adapt themselve well to their environment, to resist disease, to survive and to attain long life.

Our problems deal mainly with those who disclose *asymmetry, disproportion, disharmony, and defective adaptation of structures and functions*. In these types is often found the *soil* for development, not only of nervous and mental diseases, but for various and manifold disease processes. It is mainly these types which fill to overflowing our penitentiaries, our houses of correction, our special colonies, our almshouses, our hospitals, and our offices. Disease, in its broadest sense, with many of these types seems not to be accidental, but rather to be expected; so great is their susceptibility, so marked is their vulnerability to its processes. They do not adapt themselves well to their environment. Their resistance to disease, in the broadest sense, is often poor. Many of them succumb early in life, and proportionately few of them attain even a relatively long life.

It is in these types, more or less remote from the ideal in human development, that the scaphoid type of scapula is commonly found. It is in these types that many of the heretofore described anatomical, physiological, psychical, and moral, so-called stigmata of degeneration particularly abound. From my earliest observation of the scaphoid type of scapula, I have been impressed with its association with some of the so-called stigmata heretofore described, but I have found no particular stigma paralleling it—none approaching its frequency of occurrence.

Probably no fact in connection with the scaphoid type of scapula is at this time of greater importance than its age incidence. A consideration of its age incidence seems to indicate defective adaptation of structures and functions, which may be construed as increased disease susceptibility, in its broadest sense, in many of those in whom this anomaly is found.

Studies at the same period of time of groups of individuals in the extremes of life show that the scaphoid type of scapula is found in an extremely large percentage of the young and in a relatively small percentage of the aged, and, conversely, that the normal type is found in a relatively small percentage of the young and in an

extremely large percentage of the aged. Indeed, personal studies of groups of individuals in the several decenniums of life seem to show that with each increasing decennium the percentage of the scaphoid type decreases, while that of the normal type increases—the age incidence of the scaphoid type being approximately 80 per cent in the first and 20 per cent in the eighth decennium of life, among those who pass as normal or average individuals when chosen at random, while among those whom we have heretofore recognized, in a restricted sense, as constitutionally inferior individuals the age incidence is even greater. Much more statistical work will be necessary before an accurate curve can be charted, either for the so-called normal or for the so-called constitutionally inferior individuals of the race. Nevertheless, sufficient work has been done to indicate the age incidence of this type of scapula in the various periods of life.

In 1912 Cunningham (16) recorded observations on 1057 students in the University of California and 442 inmates of the Sonoma State Home for the Feebleminded. The student class ranged in years from sixteen to twenty-five, and in this number 72 per cent disclosed the scaphoid type of scapula; whereas in the feebleminded group, for which no age was recorded, 78 per cent disclosed this type.

Warburg (18) in 1913 studied 1000 public school children between the sixth and seventh years of age in Cologne, Germany, and found approximately 87 per cent of these to have the scaphoid type of scapula.

In a study of 236 boys, ranging in years from five to fifteen, in St. Joseph's Orphan Asylum, St. Louis, I found approximately 88 per cent to have the scaphoid type of scapula. The boys in this institution, as may well be imagined, do not compare favorably with public school children, and a few of them disclosed definite retardation, two reasons for the large percentage of this anomaly in this material.

In 1914 a study of 700 inmates of the St. Louis Infirmary (Poor House), ranging in years from forty to eighty-nine, with an average age of sixty-three, disclosed the following percentages of the scaphoid type of scapula and normal type in the several decenniums:

	Scaphoid, Per Cent	Normal, Per Cent
In the 4th	43	57
In the 5th	36	64
In the 6th	30	70
In the 7th	21	79
In the 8th	12	88

The average age of those showing the scaphoid in this material was 5½ years less than those showing the normal type of scapula.

A personal communication in 1913 from Dr. Heber Butts, P. A. Surgeon, U. S. N., gives the result of a study of 500 officers and enlisted men in the U. S. N. and Marine Corps, ranging in years from seventeen to thirty-five, most of them being between twenty and thirty, and in this number he found 32 per cent having the scaphoid type of scapula. The relatively small percentage, in the age given, of the scaphoid type of scapula in this material when compared with Cunningham's study in University

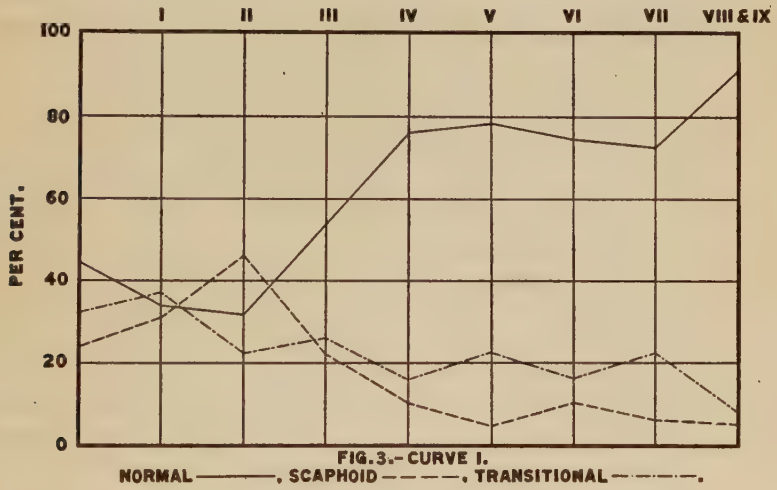

FIG. 3. Curve I. Copied from Kollert (*Wien. klin. Wocb.*, No. 51, 1912) and Used by Him to Illustrate the Age Incidence of "Normal," "Scaphoid" and "Transitional" Scapulæ in His Material of 1000 Autopsies. "Transitional" (Uebergangsform) is Identical with the "Scaphoid" Type Called "Straight."

students, in an age approximately of ten years less, is to be accounted for on the assumption that it represented picked men, and that for each man who had been accepted in the service approximately two had failed to pass the requirements.

In a recent study by Ball and Thomas (20) of 270 prostitutes in San Francisco, Cal., 81 per cent of them disclosed the scaphoid type of scapula. In a personal communication from Dr. Ball, it is stated that most of the individuals in this group were between twenty and thirty, very few between thirty and forty, and only three between forty and fifty years of age.

I am greatly indebted to Dr. Jau Don Ball for personally communicated data on the age incidence of scapulæ in an Officers' Training Camp.

There were examined 926 individuals between the ages of twenty and thirty, and of this number 360, or 38.77 per cent, had normal, and 556, or 61.23 per cent, had "scaphoid" type of scapula; whereas between the ages of thirty and forty, 472 individuals were examined, and of this number 228, or 48.3 per cent, had normal, and 244, or 51.97 per cent, had scaphoid type of scapula.

Kollert (11 and 12), in 1912, in the Institute of Pathological Anatomy and the II Medical Clinic in Vienna recorded observations on 1000 autopsies, and illustrated the age incidence of scapulæ in this material by curves.

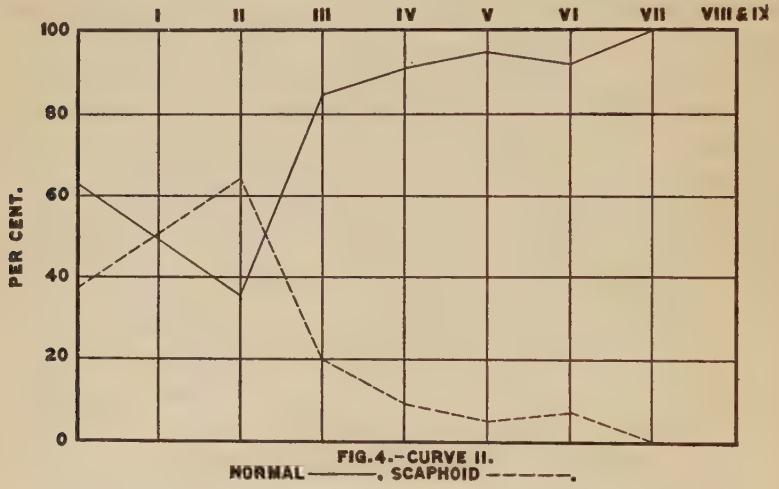

FIG. 4. Curve II. Copied from Kollert (*Wien. klin. Wocb.*, No. 51, 1912) and Used by Him to Illustrate the Age Incidence of Typically "Normal" and Typically "Scaphoid" Types after Eliminating the "Transitional" or "Straight" Types of Scapulæ in His Material of 1000 Autopsies.

Copies of two of these are shown in Figs. 3 and 4. A consideration of his curves shows that the scaphoid type of scapula, beginning with the second decennium, becomes less frequent, and the normal type more frequent with each succeeding decennium of life.

Reye (14), while offering no statistics, was greatly impressed by the great frequency with which he found this anomaly in the young as compared with its rarity in old age. *Anyone who will make only a few observations will be able to appreciate this fact.*

Commenting upon the curves just mentioned, Kollert draws the far-reaching conclusion: "*The probability of the newborn child attaining old age is decidedly greater if he has normal scapulæ than*

if he has scaphoid scapulæ." Notwithstanding the obvious deductions which seem to follow a consideration of the age incidence of scapulæ, these must not be construed harshly in applying them to the individual disclosing the scaphoid type. While most of the individuals showing this anomaly appear to be more or less remote from the ideal in human development, nevertheless there are not a few who approach this ideal.

While the age incidence of the scaphoid type of scapula seems to stamp this anomaly as a very frequent sign of hereditary or inborn weaknesses—of constitutional inferiority in its broadest sense; nevertheless *the individual possessing it should not be classed as constitutionally inferior without considering him in his entirety.* Moreover, every constitutionally inferior individual whom we may recognize as such is not the possessor of the scaphoid type of scapula, even though its natural habitat appears to be in this class of individuals.

If we accept as proven that nothing in the life of the individual after his birth can change the scaphoid to the normal type, nor the normal to the scaphoid type, then the age incidence of the scaphoid type of scapula points to the conclusion that many individuals possessing this anomaly are, in the broadest sense, the poorly adaptable, the peculiarly vulnerable, the unduly disease-susceptible, the constitutionally inferior, the short-lived individuals of the race.

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THE CLINICAL PICTURE IN SPIROCHÆTAL JAUNDICE, WITH NOTES ON THE DETECTION OF THE PARASITE IN THE CIRCULATING BLOOD

By Norman B. Gwyn, M.D.,

Former House Officer, Johns Hopkins Hospital. Former Instructor in Medicine, Johns Hopkins Medical School

THE opportunities offered in America and Great Britain for the study of that vague clinical field included in the terms Weil's disease and infectious jaundice have either been few or have not been associated with the accurate clinical means of investigation of to-day. Hence but little light had been shed on the subject since Weil's description in 1886, (1) of a disease occurring in epidemic form and characterized by jaundice and signs of an acute infection or toxemia.

To many observers the disease described by Weil has seemed the expression of some acute bacterial invasion, and their investigations have produced a heterogeneous mass of results, among which a tendency to ascribe the causal agency of the disorder to the proteus group of organisms was evident; in a résumé of the subject made for an American handbook in 1914, (2) the writer was struck by the readiness with which one author after another accepted this view, on what were certainly very unsubstantial grounds. At the beginning of the war a strong effort was made to establish the typhoid group as the cause of the epidemic jaundice seen in Gallipoli; colon bacillus septicemia expressed a French view (3); Inada, Hoki, Ido, et al., (4) by their dramatic demonstrations, have proven that the epidemic jaundices of Japan, at least, are largely, if not entirely, due to a parasite which we can comfortably see and handle, as it were, with our laboratory methods—the *Spirochæta icterohæmorrhagica.*

To the clinician, again, catarrhal jaundice with fever and signs of infection, Weil's disease, and some of the conditions diagnosed

as icterus gravis or acute yellow atrophy have appeared to have too many points in common to be properly classified as separate disorders. The discovery that the *Spirochæta icterohæmorrhagica* might be present in the milder types of jaundice may readily explain the statements that "simple or catarrhal jaundice may occur in epidemic form." "It may possibly be an acute infection" (Osler), while the frequent occurrence of cases clinically resembling icterus gravis has been a common observation in the jaundice epidemic of the war, and in many of these cases the spirochæta has been readily demonstrated.

Many opportunities to investigate the jaundices have arisen during the World War, (5) and as instancing our proper skepticism towards a revolutionary idea it may be pointed out that the theory of an epidemic paratyphoid jaundice still persists, and that as late as the spring of 1918 the extensive epidemic amongst our troops in Italy was freely spoken of as due to agents other than the *Spirochæta icterohæmorrhagica*. Difficulties in laboratory equipment probably explain the supposed clinical differences.

Segregation of the cases of jaundice began comparatively early, and after 1916 only those unobserved or undetected by the Casualty Clearing Stations drifted to our Base. No opportunity to study jaundice cases in bulk was presented to us, but from the few cases under our care we reaped an interesting harvest and, thanks to the able and active work of our laboratory under Major Ower, we had several striking séances, in one of which we demonstrated for the first time in Europe the presence of the parasite in the circulating blood, and in several others the ready transmission of the disease to the laboratory animal.

Clinically the disease is of absorbing interest, from the pale yellow type of patient with mild symptoms and infecting blood to the deep-orange hued, comatose victim, collapsed, afebrile, smeared with his black vomit and plastered thickly with a measle-like rash. Infections or affections of the biliary tract (toxic jaundice) expressed the range of the early diagnoses. Before long, however, one inclined to the idea that he was dealing with but different manifestations of the same disease.

Following are accurate details of some positive cases in which the diagnosis was established beyond a doubt by the detection of

the spirochæte in the blood, or by the commoner and easier method—the production of jaundice in the guinea pig, with clinical features of more than ordinary interest.

Case I. Sudden onset on May 2, 1916, with headache, vomiting, and abdominal pains, followed next day by intense aching of muscles. Slight fever, intense prostration.

Fever on admission to Casualty Clearing Station 99.9°. Slight jaundice noted; the spleen was palpable. Loose brown stools for one day. Vomiting, pains in leg muscles, and headache persisted. Admitted to No. 1 Canadian General Hospital on May 5th. Jaundice distinct, not intense, eyes are injected, liver is barely felt, not tender.

May 6th, nose bleeding freely, but patient is better; abdomen soft, tender on pressure; legs extremely tender to the touch, temperature falling; no herpes, and no eruptions.

May 7th. Temperature normal, jaundice already fading, patient better in every way. Stools brown and liquid.

May 8th to 12th. Jaundice has disappeared, pulse 50, liver not felt, spleen barely palpable.

May 12th to 16th. Comfortable, afebrile.

May 17th. Beginning of mild relapse. Very slight jaundice reappeared; little or no indisposition.

May 22d. Evening temperature of 101° till to-day. Liver $\frac{1}{2}$ inch below costal margin, spleen not felt. A distinct pallor is evident.

May 28th. Left hospital well.

The laboratory report is as follows: Red blood cells 5,900,000; white blood cells 12,200; polymorphonuclears 88 per cent; lymphocytes 11.5 per cent; eosinophiles .15 per cent.

Agglutinations against β typhosus, paratyphoid A, and paratyphoid B are negative. Inoculated, typhoid only, several years ago.

Urine. May 5th to 6th. Bile present, 1020, albumin positive, casts of all sorts, bile-stained, no sugar, leucin and tyrosin not tested for. May 7th. Bile faint, albumen trace, many casts. May 8th to 9th. Bile absent, albumen trace, few casts. No spirochætes found in urine at any time. Feces brown, liquid, no excess of fat noted, negative for members of the typhoid group.

Blood cultures negative for bacteria anaerobically and aerobically on May 4th, 5th, and 6th.

Blood of May 5th: 10 c.c. allowed to clot, serum removed by sterile pipette, centrifuged at once while warm. A dozen actively motile spirochætes found after short examination. Stained specimens (Fontana) of

precipitate show several distinct spirochætes. There were no guinea pigs in the district at this time.

May 6th. Blood to-day showed only a few spirochætes.

May 7th. Temperature now normal. Blood of this date inoculated into guinea pigs did not produce jaundice or illness in the animal.

Case II. Admitted to No. 1 Canadian General Hospital, August 23, 1916. Onset five days ago with rigor, intense pain in muscles requiring morphine for relief; vertigo, nausea, vomiting, but no abdominal pains or diarrhea.

On fourth day jaundice; muscle pain intense.

On fifth day jaundice more marked, bleeding from the nose; tongue is moist, however, and patient does not seem an ill man. Eyes not injected, no abdominal pains, liver dullness reaches costal margin, but liver is not palpable, spleen not palpable, no glandular enlargement.

On sixth day, temperature 102°, lungs and heart clear, mouth and gums clean, not bleeding, tongue moist. Condition good; there is still some aching of muscles.

Seventh and eighth days, swelling and pain developed in right knee. Temperature dropped suddenly on eighth day; jaundice already fading. Uninterrupted recovery. Laboratory records were as follows: Red blood cells 4,000,000; white blood cells 12,000; polymorphonuclears 75 per cent; lymphocytes 24 per cent; transitionals 1 per cent.

Agglutinations.

	1/50	1/100	1/250	1/500
Typhoid.....	+	+	+	+
Paratyphoid, A.....	+	+	+	0
Paratyphoid, B.....	+	0	0	0

Patient injected with "triple vaccine" in March and April, 1916.

Urine. August 23, 1916. Bile, positive, 1030; albumen, trace plus; sugar 0; hyaline and granular casts.

August 25. Bile positive, 1020; albumen, trace plus; few hyaline and granular casts.

August 26. Bile positive, 1018; albumen, few casts.

August 30. No bile; no albumen, and no casts.

Examination of blood by dark field illumination negative for spirochætes on August 23 and 24.

Inoculation of guinea pig on August 23; 5 c.c. of blood intraperitoneally. Pig died of jaundice after eight days, with typical post-mortem findings. Numerous spirochætes in liver and heart's blood. Inoculation from this pig's liver and blood produced fatal jaundice in second pig, and spiro-

chætes could be demonstrated in a drop of blood taken from the animal's ear before death. Pig No. 2 produced fatal jaundice in a third and numerous cases of jaundice in guinea pigs were produced in the district for the various laboratories.

Blood cultures and stool cultures showed no member of the typhoid group.

Case III. Admitted to Surgical Ward April 28, 1916, as cholecystitis. Slight jaundice, vague abdominal pains.

Temperature normal by next day, 29th. Seemed well. History: Taken suddenly ill two weeks previously with vertigo, headache, vomiting, and the subsequent development of slight, centrally situated, abdominal pains; muscle pain not a feature; remained afebrile till May 8th, when temperature began to rise and a faint jaundice tinge appeared. Eyes were not injected, patient seemed distinctly irrational; heart, lungs, and abdomen negative on examination; liver reaches from the sixth rib to the costal margin, neither spleen nor liver are palpable, nor is there tenderness over these organs on palpation; the legs are not tender.

May 9th. Quite delirious, jaundice distinct but not deep, yellow, not orange; there is no bleeding anywhere; mouth clean, tongue moist, eyes not injected; no abdominal pain or tenderness; temperature is rising.

May 11th. Temperature 104.5°, eyes staring, delirium acute, but jaundice has not deepened. No bleeding from gums or mouth, heart and lungs are clear.

May 12th. Is better, mind clearer, neither liver nor spleen can be felt.

May 13th. The slight jaundice is clearing. Temperature fell to normal in twenty-four hours, uninterrupted recovery. Laboratory records were as follows:

Feces colored, negative for excess fat, for parasites, and for members of the typhoid group.

Urine. May 8th. 1020, bile-stained; alb. ?; sugar 0; a few granular and epithelial casts.

May 9th. A complete change in twenty-four hours. Bile positive. Albumen now in quite large amounts. Sugar 0. An enormous number of casts of all sorts.

May 10th. Albumen still in marked amounts, casts in abundance. Bile-stained.

May 13th. Urine absolutely clear.

No spirochætes in the urine in five different examinations between May 8th and May 23d.

Blood. Agglutinations against β typhosus, paratyphoid A and paratyphoid B negative: Red blood cells 4,480,000; white blood cells 11,200;

polymorphonuclears 75.5 per cent; lymphocytes 22 per cent; transitionals 3.5 per cent; eosinophiles .5 per cent; basophiles .5 per cent.

The low leucocytic count at the height of the fever is to be observed.

May 8th. Blood negative for spirochætes; culture negative.

May 9th. A few spirochætes of the very irregular types pictured by the Japanese observers were found. Animal inoculation gave no results.

Such, in brief, are the details of some of our cases in which the presence of the parasite could be determined. At the time of death of two well-marked cases of icterus gravis neither dark field illumination nor animals were available. There has been abundant proof, however, of the ready transmission of an infectious jaundice from this type of the disease, and a fatal afebrile case in an adjoining clinic gave opportunity of demonstrating not only the transmission of the spirochætes to animals, but also the presence of the organisms in the scrapings from the patient's liver. It is to be noticed in passing that so far in the writer's experience, even in the severest types of icterus gravis, he has never seen the post-mortem picture of acute yellow atrophy with proved spirochætal association. The possibility of this association must, however, be borne in mind.

As mentioned before, no large number of cases of febrile jaundice came under observation. Segregation in special hospitals and retention in the Casualty Clearing Stations during the acute stages of the disease precluded our ever having under our care any but convalescents or those who, jaundice-free in the early days of their disorder, passed through the forward areas diagnosed vaguely as some abdominal or febrile complaint. In fourteen cases we were able to make more or less complete chartings of the disease, and the clinical findings in these amply repaid us for our work and quickly gave us a new viewpoint upon our preconceived ideas of jaundice.

From the many conditions and multiform appearances one may with advantage select certain points of interest as bearing upon epidemiology, symptomatology, physical signs, and diagnosis, the points most useful in consideration of any disease from the side of the clinical observer.

1. Epidemiological Details. (*a*) In no case could our patients call to mind other instances of jaundice among their mates. Either the disease

never assumed the proportion of a great epidemic, or the victims left the line before the distinguishing features of the disorder had developed. (*b*) The disease seemed pre-eminently a front-line condition, occurring in men the majority of whom are constantly in contact with the now proven common carrier, the wild rat (Jobling et al.): (8) 9 cases from the trenches, 2 from batteries, 2 from forward area motor corps, 1 from field ambulance. (*c*) No seasonal incidence could be fixed upon. The majority of our cases were admitted between December and May. It is to be remembered, however, that by the summer of 1916 more careful segregation of cases began to be practiced.

2. Some Details of the Symptoms and Physical Signs. *Features in Association with Onset.* (*a*) For 6 who gave the definite history of a sudden acute onset there were 7 in whom the development of the disorder could best be described as gradual. One case is noted as "only semiconscious on entry, mode of onset not described at Casualty Clearing Station."

(*b*) *Chill.* A definite chill was the first sign of illness in 7.

(*c*) *Prostration and Headache.* So marked as to be indicated "double plus" in our columns, these two early symptoms stood out prominently in every instance, even in cases showing but slight fever and but little staining of the skin.

(*d*) *Vertigo.* In 6 of the 14 cases this was an acute symptom of the onset.

(*e*) *Nausea, Vomiting, Diarrhea, and Abdominal Pain.* Nausea and vomiting occurred early in every case. In two instances vomiting did not begin till the third day; in one instance it persisted as a profuse black vomit till the fatal termination eight days after onset. Diarrhea was a less constant symptom; it was absent in 6 cases, present in 8.

Abdominal pain, usually central, though in 2 cases referred to the liver, was absent in only 2 of 14 patients. In 2 instances it was designated as severe, but at no time did the condition merit the description of an acute abdomen; its disappearance with the cessation of nausea, vomiting, and diarrhea within the first week is usual. In a fatal case its persistence was due to acute inflammation of duodenum and ileum. The pain may reappear with a relapse. General abdominal tenderness was present in all; 2 patients referred the greatest point of sensitiveness to the region of the gall bladder, one to the epigastrium; rigidity such as is felt over an abdominal inflammation was never observed.

(*f*) *Muscle Pains and Myositis.* Prominent among the early symptoms and possibly due to the invasion of the muscles by the parasite with subsequent reaction, are the muscle pains; hardly enough insistence has been placed upon this symptom, and to limit their distribution to the muscles of the calves, as is so frequently done, gives a wrong impression of their

extent and severity; soreness of all muscles with an unusual degree of tenderness occurs, and in only 1 case was its absence noted. Soreness of the muscles of the arms, trunk, and thighs is especially common. In the following case the condition of the thigh muscles opens up a fruitful field of conjecture.

Case admitted February 12, 1916. Sick for six days with weakness, vertigo, stiffness of both legs, which is increasingly painful. Jaundice after the third day.

February 13th. Patient severely ill, pains in the thighs are intense, the left thigh is swollen, tense; there is edema of the skin, which is not perceptibly reddened.

February 17th. The extreme tenderness has persisted, pulses are present in both ankles, there is no sign of venous thrombosis. Leucocytes 13,000. Jaundice deep orange. The right leg has now become swollen, tense, and edematous. Patient is prostrated and ill. The swelling and pain is such that deep-seated suppuration is suspected. Temperature, however, has been of steady type and never above 100°. Pulse only 100.

February 24th. Pain and swelling have disappeared. Slight pain recurred in both legs with a relapse a few days later. Recovery.

In an earlier article (Gwyn and Ower) we mentioned the fact that "in a fatal case of infectious jaundice a peculiar muscle degeneration had been described by Captain Pringle," the then pathologist at Etaples. A few months previously a remarkable case of generalized inflammation of the muscles had been reported from our hospital by Colonel Finlay. The onset in this case was with nausea, vomiting, and severe diarrhea. The case notes are here given.

Case, Private M., Age forty-five. Admitted November 12, 1916, with acute soreness and swelling in the muscles of arms and legs. Has always been well, denies syphilis, no history suggestive of tuberculosis, malaria in India, and history of acute rheumatism ten years ago and again last winter. Is careful of his diet and of the water he drinks; there has been no pork or sausage in the meat rations.

Present illness began four to five weeks ago with nausea, vomiting, and severe diarrhea. This lasted several days; thinks he had fever at the onset. After a few days muscle soreness began and has continued. Forearms and arms are sore, swollen, and tense, there is some soreness of the muscles of the calf and of the chest muscles on breathing. Nowhere is there any redness of the skin; the eyes have been swollen on several occasions; there has been slight cough.

On admission there was no fever, pulse quiet, respirations quiet, there was no swelling of the eyes, bowels regular, no abdominal pains. Heart and

lungs are clear, hands glossy, swollen, somewhat congested from the coldness of the tents; skin is cold; arms and forearms are tense, boggy, and brawny, very sore. Condition suggests muscle infiltration. The skin is incised, but does not appear edematous. A piece of muscle was removed from the right forearm. No swelling of the deltoids. The outer sides of both lower legs are stiff and sore, the quadriceps-extensors are very firm, sore, and tender to the touch, abdomen negative. By the end of the week patient very weak, cyanosed, pulse poor, a great deal of expectoration, and lungs are full of sonorous râles. There is no dullness, though resonance is impaired at bases, heart sounds very feeble, abdomen quite flat, but patient complains of severe pains in the lower-middle abdominal region. There is no rigidity, bladder is found empty. Patient failed quickly, and died that evening.

Temperature never above 97°; pulse 112 to 140; respiration 16 to 40.

The question as to the origin of the myositis was always before us. Stools were carefully examined, and the piece of muscle taken from the forearm was searched for the trichina spiralis. Cultures were also taken from the exposed muscle tissue at the same time. The laboratory report shows that we were dealing with a condition evidently not related to trichinosis, the blood count showing no trace of eosinophilia, stools being negative and the muscle degeneration proving something of quite a different nature.

The urine, negative on admission, eventually showed albumen and many casts. The count of the white blood cells was 24,500. Polymorphonuclears 78 per cent; small mononuclears 13 per cent; large mononuclears 6 per cent; transitionals 2 per cent; eosinophiles 1 per cent.

The feces appeared normal and blood cultures and muscle culture remained persistently negative. The autopsy shows a negative condition of liver, stomach, intestines, pancreas, bone-marrow, spleen, and adrenals; a well-marked edema of the lungs. There is a large number of small white plaques on the visceral pericardium; the heart is slightly enlarged, valves clear, the muscle distinctly pale. Distinct swelling of forearms, hands, thighs, and calves persists. The skin still pits on pressure. The muscles of the body appear everywhere brownish rather than red, the cut surfaces having a shiny hyaline appearance. This is particularly marked in the muscles of the abdominal wall and in the psoas muscles. A large hemorrhage is found in and about the sheath of the left psoas muscle and extending into its depths. This probably caused the severe pain of the night before. Both kidneys are swollen, the cortex gray red, the capsule not adherent.

Microscopically the muscles show very marked changes. In some areas the whole muscle fiber has disappeared, leaving only the membrane. In

others there is only swelling and loss of striation, in still others there is marked vacuolation. There are innumerable small and large hemorrhages into the interfibrillar spaces. There is no evidence of leucocytic infiltration around the degenerating areas. No suspicion of spirochætosis was entertained at this time, and special staining was not carried out. The microscopical picture in this case was found to be strikingly similar to that described by Captain Pringle in his case of fatal jaundice with muscle degeneration.

The proof of the existence of spirochætal infection without jaundice is given in Sir Bertrand Dawson's article on "Infectious Jaundice" (6). We quote an abstract of the case, which seems convincing:

"Case showing sudden onset with body pains, frontal headache, photophobia and vomiting, temperature first day 104°, pulse 100. Conjunctivæ injected, herpes labialis, spleen not felt. Albuminuria very marked, no bile in urine. No jaundice, persistent bilious vomiting. A relapse of fever took place after several days of apyrexia. On the third day of illness 2½ c.c. of blood produced typical jaundice in the guinea pig and spirochætes were present in abundance in the liver."

Myositis of infectious type is especially frequent in Japan. It would be interesting to know if it prevails in the regions where jaundice is described as most prevalent. To the writer the chain of evidence—clinical myositis in jaundice, acute degenerative muscle changes in fatal jaundice, the case of generalized fatal myositis with no evidence of trichinosis or suppurative changes, proven spirochætal infection with muscle pain but without jaundice, and the probable existence side by side of the two rather rare diseases —seems most convincing. One will await some positive spirochætal findings in these cases of myositis with expectant interest.

(*g*) *The Jaundice and Eruptions.* In no case was the jaundice observed before the third day of illness; two of the patients had run seven days before the change of color attracted attention. In only one of the three spirochæte-positive cases was the jaundice of a deep hue; its reappearance during relapse was constant. The deep jaundice in one relapse case did not fade in the interval. Both of the cases ending fatally were of a deep orange hue on admission. A green jaundice has never come to our notice; orange, rather than yellow, is the prevailing color. The estimation of

the duration of the discoloration was impossible under our evacuation demands.

An erythematous scarlet flush on the orange base, more marked on the face, was charted in half the cases, herpes labialis was present in four (28 per cent). In one of these cases the herpes was hemorrhagic. In three cases a striking clinical picture was observed when a diffuse splotchy rash, measle-like in its extent and grouping, covered the already deeply orange-tinted victims. Typical spider-angiomata developed in the skin in one case. The injection of the conjunctivæ, considered so important in differentiating the infectious from other forms of jaundice, was regularly present.

(*h*) *Mental Condition and Nervous Symptoms.* The 2 fatal cases remained in a comatose state from the day of their admission; 4 cases were distinctly delirious at the height of the disease. A mild delirium preceded and accompanied the relapse in 1 instance; 5 cases were described as being markedly drowsy while in the ward. One of the fatal cases died in convulsions, presumably following or associated with suppression of urine.

(*i*) *Hemorrhagic Manifestations.* Bleeding from or into various parts of the body is evidently as common a feature of infectious jaundice as it is of jaundice due to other causes (Larrey, Carville, Weil) (6). In many of our cases hemorrhages were a distinct feature: 6 bled from the nose, 3 showed conjunctival hemorrhages, 2 bled freely from the mouth and gums, 2 passed blood by bowel, 1 coughed up blood in distinct amounts, and had also hematemesis; 1 showed hemorrhage into his pericardium at autopsy.

As opposed to the experience of most observers, we noted but 1 instance of purpura amongst our cases.

(*j*) Physical signs other than the swollen muscles, jaundice, eruptions, and hemorrhages are rare. One dry pleurisy and 1 lobular pneumonia represented the findings as regards the pulmonary system; in 2 convalescents the pulse rate dropped to 52 and 42; 1 fatal case showed marked cardiac irregularity due to omission of ventricular cycles. Neither of the 2 afebrile fatal cases showed bradycardia; there were 2 instances of mild arthritis.

The condition of the liver, spleen, kidneys, and feces merits a few words. The liver and spleen were carefully and repeatedly examined. We can say positively that enlargement of these organs sufficient to make them easily palpable was not the rule in our cases. Our findings may be tabulated as follows:

	Liver	Spleen
In 11 cases	0	0
In 2 cases	+	+
In 1 case	+	0

In no case was the enlargement of the liver or spleen such that it could be called gross. Tenderness over the liver was noted in 3 instances and over the spleen in 2. In neither of the fatal cases was the size or weight of the liver appreciably altered, and the spleen was reported as small and normal in appearance. In 1 only of the 3 cases positive as regards examination for spirochætes could the liver be felt, and then only with difficulty.

The Condition of the Kidneys. The severe degree of nephritis is generally assumed to be a cardinal part of the disease. Albuminuria with casts is regularly seen, but in our experience was a condition belonging to the few days of the acute febrile reaction. It is probably more marked in the more severe cases. In no case that recovered were the signs of acute nephritis present for more than six days; reappearance of albumen and casts was seen with the relapse as a general rule, occurring within twenty-four hours in 1 case. One relapse case remained albumen-free in the second bout of fever; disappearance of albumen and casts within twenty-four hours after the temperatures fell to normal was observed. One fatal case, afebrile, had the following urinary report and post-mortem findings:

October 23 and 24, 1916, by catheter, 3 oz. Bile plus, albumen double plus, sugar 0, casts of all sorts in abundance, and blood cells.

October 25th, by catheter, 57 oz., 26th, 64 oz., 27th, 53 oz. Bile plus: 1014, albumen trace plus, sugar 0, few granular casts.

October 28th, autopsy. The left kidney is larger than the right, capsules strip readily, there is no pouting of the cortex which does not seem swollen, and the cortical surface, though noted as congested, appears to be in remarkably good condition.

In the second fatal case, afebrile, "albumen with many casts of all varieties, were the findings during life," while at autopsy the signs of an acute diffuse nephritis were found.

In the urine of the 12 remaining cases bile and hyaline and granular casts were present in all; albumen in all but 1. Blood was demonstrable in 2 cases. Sugar was uniformly absent.

In only 3 cases was albumen present in amounts sufficient to be marked +. On 2 occasions leucin and tyrosin were looked for, but with negative results. In but 1 case did we think that the spirochæte-like bodies found in the urine could be considered as the spirochæte of jaundice. We were unable to prove this at the time.

In 9 cases it was apparent from the color of the stool that bile was reaching the intestines. One o fthese is the fatal case described as showing intense duodenitis and enteritis (not every inflammation about the diverticulum suffices to block it); the "gall bladder and bile ducts are free, bile can be squeezed into the intestine," is the autopsy note.

In 3 cases the feces were quite white and fatty. In 2 they were of a grayer color, but were greasy and showed microscopical evidence of fat. The 3 cases positively spirochætal had brown-colored stools.

(*k*) *The Blood Picture.* But few complete records were obtained. The hospital was at one time without blood-examining apparatus.

The finding in one spirochæte-positive case:

White blood cells 12,300; polymorphonuclears 75 per cent; lymphocytes 24 per cent; eosinophiles 1 per cent.

Agglutinations. (Inoc. T. A. B. (2) four months ago.) Typhoid T, 1/500; paratyphoid A, 1/250; paratyphoid B, 1/50.

The findings in a second were: Red blood cells 5,900,000; white blood cells 12,200; polymorphonuclears 88 per cent; small mononuclear 9.5 per cent; large mononuclear 2 per cent; eosinophiles .5 per cent.

Agglutination against β typhosus, paratyphoid A and B was negative. The patient had never been injected with vaccine.

Records of other cases were:

	Red Blood Cells	White Blood Cells	Differential Count. %
1.	3,328,000	17,600	pmn. 85.5; lym. 11.5; tr. 4; eos. 4
2.	5,976,000	7,000	pmn. 55 ; lym. 38; tr. 6; eos. 1
3.	4,480,000	11,200	pmn. 73.5; lym. 20; tr. 3.5; eos. 5
4.	0	14,000	pmn. 79; lym. 21; tr. 5; eos. 3
5.	0	5,200	pmn. 64; lym. 29; tr. 5; eos. 1

No cells foreign to the normal blood were seen. Absence of anemia in the early stages with a moderate increase in the white blood cells, but with no constant change in the differential counts, seemed to be the most usual picture in the cases examined.

Course of the Disease—Temperature—Termination. Recovery is the rule. By the fourth and fifth day improvement in all directions takes place. The 2 fatal cases, both with the symptoms of icterus gravis well marked on admission, never rallied and died on the seventh and eighth day of their illness respectively. Both showed a curious lack of febrile reaction. The cases not complicated with a relapse quickly regained their normal state. The relapse cases were all noted as showing a persistent pallor and weakness during convalescence. Complications are few. One myositis, 2 instances of arthritis, 1 pleuritis, 1 broncho-pneumonia comprised the range of secondary accidents.

In 8 of the 14 cases the acute febrile period of the illness showed but a single phase. It is probable that both the fatal cases had some short spell of fever before the subnormal reaction became evident. The usual duration of the fever wave was from three to eight days. Six cases, or 37.5 per cent,

showed definite evidence of relapse with recurrence of fever, and this secondary fever was in 5 cases of greater duration than the primary wave; with the febrile recrudescence, deepening of the jaundice, headache, delirium, muscle pains, abdominal pains, bleeding at the nose, and herpes were observed to occur. The prostration seemed less than at the onset of the disease; vomiting and diarrhea were conspicuous by their absence. In 2 cases both liver and spleen could be more distinctly palpated during the relapse. In 1 of the 3 positive spirochætal cases the parasite was found during the fever of relapse.

In 2 instances crisis-like falls of temperature were seen to occur within twelve and twenty-four hours, but in the majority of cases a gradual rise and fall of the fever was noted. The highest temperature recorded was 104 (2) (in a relapse). The low temperatures of the icterus gravis-like cases have been already commented upon.

Some pulse rates coincident with elevated temperatures were the following:

Case	Temperature	Pulse rate
I	104.2°	100 to 80. Positive spirochætosis.
II	102.°	76
III	103.°	88
IV	102.5°	100
V	103.5°	104

In both fatal cases, comatose and deeply jaundiced, an average pulse rate of 80 to 90 was recorded during their afebrile course. In 1 a sudden rise to a 140 per minute was recorded for twenty-four hours before death. It can be seen that in both the febrile and afebrile type of cases a certain degree of inhibition of the pulse rate is evident.

Notes on the Detection of the Parasite in the Circulating Blood. In no great number of human infections is the laboratory able to demonstrate living protozoan parasites in the circulating blood. Relapsing fever, malaria, trypanosomiasis, trichiniasis have thus far represented our successful performances in this line, and to have another possible field in view should not fail to arouse our utmost endeavor.

The natural tendency is to rely upon animal inoculation for the production of jaundice, and the subsequent demonstration of the parasites in the animal's liver, kidney, or heart's blood, since in this way the demonstration is undoubtedly easier, and probably more certain. Dark field illumination is necessary. In our 2 positive cases

we drew 5 to 10 c.c. of blood, collected the serum after clotting, rapidly centrifuged it and with no more trouble than is frequently experienced in demonstrating the estivo-autumnal type of malarial parasite were able to find and follow a dozen spirochætes in their wanderings over the field. As further showing the parasite's right to be called a blood parasite, we were able to find living specimens in a drop of blood taken under simple precautions from the ear tip of an infected animal.

The Japanese observers were successful in detecting the spirochæte in the blood of patients on six different occasions. Positive blood findings are also reported by Salvaneschi (9) in the Italian epidemic.

We were successful in finding the *Spirochæta icterohæmorrhagica* in the urine in only 1 case. In this connection two points are to be remembered: That nonpathogenic spirochætes are regularly found in the secretion about the corona glandis and in the meatus, and that the nuclear network of the cells seen in cellular casts may be most confusing when examined with the dark field illumination; urinary spirochætosis in febrile jaundice undoubtedly occurs, however, and the transmission of the disease to animals by inoculation of infected urine seems to have been done successfully on many occasions.

With stained specimens of precipitated serums we were fortunate in being able to demonstrate several well-formed spirochætes, and we feel that further successful results were forestalled only by the late period of the disease at which we were compelled to make our examination. The transmission to animals by intraperitoneal inoculation of 2 to 3 c.c. of whole blood, taken early in the disease, is easy, and is followed by a large percentage of positive results. The jaundice in the pig is of no uncertain hue and is readily seen in the injected conjunctivæ or by examining the skin at the root of the hairs. The parasites in the liver may be seen under the microscope at times almost like an actively swarming mass; further details of pathology and histology in both man and animals will appear in a paper by the writer and Major Ower, with whom this study of infectious jaundice—rather superficial from necessity, owing to our surroundings and conditions—was taken up. With him I experienced the pleasure of exploring this chapter of clinical medicine, hitherto

but vaguely understood by most of the observers on the Western Front. With him I feel that the laboratory side of infectious jaundice offers a fertile field for both the clinician and the laboratory worker and one that must materially help in unraveling that tangled chain of the jaundices, linked loosely together, in which we find so many conditions ranging from simple catarrhal jaundice to the jaundice with acute yellow hepatic atrophy.

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For the brief bibliography the writer must make apology. Situated as he was at the time of writing in a remote corner of France, in a dismantled hospital, he was quite unable to consult the enormous literature which now exists on the subject.

RECENT DEVELOPMENTS IN THE THERAPEUTICAL USE OF OXYGEN

By J. S. Haldane, M.D., F.R.S., Oxford

IT has been known for long that the administration of oxygen sometimes produces temporary amelioration of the symptoms in cases where dyspnœa or cyanosis is present; but until the experience of the war in the treatment of gas-poisoning cases, and the physiological investigations to which this experience has given rise, there was very little knowledge as to the serious therapeutical use of oxygen, or the indications for its use. In the present paper I shall endeavour to present a short account of the new light which has been thrown on this subject, including a summary of clinical and experimental work carried out by Lt.-Col. J. Meakins of McGill University, Capt. J. G. Priestley of Oxford, and myself, with the support of the Medical Research Committee. This work was initiated at the Canadian General Hospital, Taplow, through its Consulting Medical Officer, Sir William Osler.

In order to understand the therapeutical use of oxygen it is absolutely necessary to have some understanding of both the immediate and remote effects of want of oxygen. Our direct knowledge of this subject is derived partly from laboratory experiments, but largely also from observations of the effects produced by the want of oxygen experienced at high altitudes owing to the rarity of the air, and in carbon monoxide poisoning owing to interference with the oxygen-carrying power of the hæmoglobin. The evidence is absolutely conclusive that in both these cases the characteristic effects are due simply and solely to want of oxygen.

The immediate effect of an almost complete cutting off of the oxygen supply to the lungs is, of course, loss of consciousness followed within a minute or two by convulsions and death. With a very moderate diminution, sufficient to produce only very slight cyanosis, the first effect is usually a marked increase in the breathing. This soon falls off, however, and the breathing settles down to a comparatively slightly increased depth or rate, which may not be at all

noticeable. At the same time the cyanosis of the lips, etc., becomes more noticeable, since the diminished breathing brings less oxygen into the lungs.

When the deficiency of oxygen is produced gradually there is no prominent increase in the breathing, and increased breathing is not a prominent symptom in the case of men gradually ascending to dangerous heights, gradually absorbing formidable amounts of CO, or gradually coming under the effects of diminished absorption of oxygen by the lungs or of a diminished circulation rate, with consequent diminished oxygen percentage in the blood of the systemic capillaries. The normal stimulus to respiration is not deficiency of oxygen, but excess of CO_2 in the arterial blood, and this stimulus depends on the action of carbonic acid in diminishing the alkalinity, or increasing the hydrogen ion concentration, of the blood. The most prominent action of this stimulus is to increase the *depth* of the breathing, as occurs during healthy and moderate muscular exertion. The first effect of the abnormal stimulus due to want of oxygen is to increase the sensitiveness of the respiratory centre to carbonic acid. Hence at first an excessive amount of CO_2 is washed out from the blood and tissues by increased breathing. When this excess is got rid of the breathing quiets down again to a great extent, as mentioned above. When the breathing is, during rest, persistently increased in depth without any signs of anoxæmia, a condition of acidosis (due to renal failure, diabetes, or some other cause) must be suspected, and oxygen administration will of course be of no use, while treatment by large doses of a suitable alkaline substance such as sodium bicarbonate may be required. Such treatment would of course be harmful in a case of hyperpnœa due to want of oxygen. A respiratory symptom which is very apt to appear in conditions of slight oxygen want is, however, periodic breathing. At high altitudes this is practically a normal phenomenon until, after two or three days, adaptation is established.

The further symptoms produced by continued slight want of oxygen must now be carefully considered, as they are of great practical significance in medicine. In the first place there is distinct impairment of mental faculties, often showing itself in manifestations similar to those of alcoholic intoxication. The powers of judgment, self-control, and memory are distinctly impaired. After

some hours there is nausea, headache, and often vomiting or diarrhœa, along with great mental depression—the ordinary symptoms of "mountain sickness" or of slight CO poisoning. The occurrence of these delayed symptoms depends on the duration of exposure to want of oxygen, and not merely on the extent of the exposure. If the exposure has been sufficiently long, though very slight, they still occur, even if meanwhile their cause has been removed. After slight CO poisoning the headache, etc., are quite commonly delayed till after the patient has returned to pure air and has got rid of most of the CO from his blood. The delayed symptoms of oxygen want in CO poisoning are mainly responsible for the time-honoured myth that CO remains for long periods in the blood; and the delayed symptoms of mountain sickness in airmen are similarly responsible for a more recent pathological myth.

When the want of oxygen is more serious both the immediate and delayed symptoms are of a far more formidable character. Hyperpnœa is more evident; periodic breathing usually gives place to regular breathing: consciousness is greatly impaired or lost: the pulse becomes frequent and feeble. But what must be specially emphasised is that the longer the period of want of oxygen lasts the greater is the progressive damage done to the central nervous system, heart, and other organs, and the slower and more difficult does recovery become. Nothing is more striking, for instance, than the fact that a man who has been rendered unconscious for some hours by CO cannot be recovered at once if the CO is rapidly removed from his blood and the full normal oxygen supply to his tissues re-established. He may never regain consciousness, and may sink hopelessly owing to the damage which his organs have received during the exposure to want of oxygen. The lesson of carbon monoxide poisoning is one of the most important in the whole of pathology; and exactly the same lesson has been taught again and again in connection with the want of oxygen caused by irritant gas-poisoning or pneumonia. When a patient with blue or leaden-coloured lips becomes of a normal colour on administration of oxygen, and yet does not show other marked signs of immediate improvement, his symptoms are often grossly misinterpreted, just as in CO poisoning the after-effects of want of oxygen are often taken as evidence of the continued presence of CO in the blood.

The practical upshot of what has just been said is that a deficient oxygen supply to the body, if allowed to continue, is undoubtedly a matter of very serious moment to a patient, and should be prevented if this is at all possible. The recent clinical and experimental observations have shown that far more can be done in this direction than formerly seemed practicable.

Apart from CO poisoning and the similar conditions produced by poisons such as nitrites, which act on or even destroy hæmoglobin, want of oxygen may be produced in two ways. In the first place the circulation may be slowed down owing to failure of the heart-muscle, valvular defect, or a variety of other causes. The result of this must be that in consequence of the slowing the blood in the systemic capillaries tends to become more venous. The excess of CO_2 can be compensated for by increased breathing, so that the arterial blood contains less CO_2 than normally. But deficiency of oxygen cannot under otherwise normal conditions be compensated for in this way, as the hæmoglobin of arterial blood is almost saturated with oxygen, so that abnormally increased breathing in a healthy person cannot appreciably increase the saturation. Hence anoxæmia in the systemic capillaries must result. Observation of the colour of the lips, etc., in chronic heart cases suggests that the tissues may gradually become acclimatised to a certain amount of anoxæmia, but this cannot be expected in acute cases, so that very serious results must be expected.

In the second place want of oxygen may result from failure in the normal oxygenation of the blood in the lungs. The oxygenation may be hindered by thickening, or clogging with exudation, of the extremely delicate layer which separates the blood from the alveolar air. At places where complete consolidation occurs it appears that the pulmonary blood stream is diverted. The partial pressure of oxygen in the venous blood entering the lungs is about 6 per cent of an atmosphere, according to very exact measurements which I have made in man, and appears to be very delicately regulated. In the alveolar air the partial pressure is about 13 per cent. The difference, 7 per cent, is the initial diffusion pressure available for driving oxygen inwards, and is far more than sufficient during normal resting conditions, since even during hard work, when perhaps eight or ten times as much oxygen has to enter

the lungs, the arterial blood is nearly as fully saturated with oxygen.

In poisoning by lung-irritant gases such as phosgene the first serious symptoms are those of anoxæmia, and occur at first during exertion (with suddenly fatal results in some cases), and later even during rest. The anoxæmia is easily recognised, not only by the very formidable symptoms which accompany it, but by the blue or leaden-gray colour of the lips and face. Examination of the blood shows at once that the abnormal colour is simply due to the fact that the hæmoglobin is not oxygenated. It is not otherwise chemically altered in the slightest degree. The natural interpretation of this anoxæmia was that the oxygen could not penetrate quickly enough through the obstruction due to swelling and exudation; and for this reason I devised an apparatus which has been very successfully used in the British and American Armies for the economical continuous addition of oxygen to the inspired air. This apparatus was afterwards described in a paper on Oxygen Administration in the *Brit. Med. Jour.*, February 10, 1917. By adding a comparatively small percentage of oxygen to the inspired air one can enormously increase the available diffusion pressure through the alveolar walls. By keeping up this condition until recovery has so far progressed that the patient is again able to breathe air without suffering from anoxæmia he is tided over the period of danger. The therapeutical results obtained, as carefully investigated by Lieut.-Col. Douglas of Oxford and other medical officers on the Western front, were very striking.

The further experiments and observations made at the Taplow Hospital showed, nevertheless, that the explanation just given was by no means complete, and that oxygen administration has an additional effect of far more wide-reaching importance in ordinary practical medicine. A large proportion of men suffered from chronic effects of gas-poisoning. On investigating these cases Colonel Meakins, Captain Priestley and I found that the breathing on exertion, and in many cases during rest, was of a totally abnormal character in respect that it was extremely shallow and correspondingly frequent. We found the same type of breathing in military cases of "Irritable Heart" or "Disordered Action of the Heart" of "Neurasthenia," and "Shell-shock." We also found that in these

cases the distress on exertion was ameliorated by breathing oxygen. We then found that on restricting in normal persons the depth of breathing, so that a compensatory increase in frequency resulted, symptoms of anoxæmia were produced, the first of these symptoms to appear being Cheyne-Stokes breathing of the ordinary clinical type. On adding a little oxygen to the inspired air the Cheyne-Stokes breathing was rapidly abolished, just as occurs in ordinary clinical cases of Cheyne-Stokes breathing, as was discovered at Guy's Hospital many years ago by Pembrey and Allen. During the anoxæmia the alveolar air, when investigated by the well-known method introduced in 1903 by Captain Priestley and myself, showed an average *increase* in oxygen percentage. It then became evident to us that the explanation of the anoxæmia lay in an anatomical fact which was clearly described some years ago by Professor Arthur Keith. During an inspiration the lungs do not expand evenly all over, but open out gradually, something like the leaves of a Japanese fan, commencing at the surfaces of the diaphragm or chest-wall which move during respiration. In consequence of this fact the ventilation of different parts of each lung must be very uneven during shallow respiration, as only parts of the lung are expanded. Thus the air is left relatively stagnant in some parts, while in other parts there is over-ventilation, owing to the increased frequency which accompanies the shallow breathing. A sample of alveolar air represents only the average over the whole lungs.

As was shown by Captain Priestley and myself, the breathing is under normal conditions so regulated that the partial pressure of CO_2 in the alveolar air, and consequently in the arterial blood, remains steady. With shallow breathing the increased ventilation of the over-ventilated parts of the lungs washes out from the blood a correspondingly increased proportion of CO_2. That this must be so can be seen at a glance from the dissociation curve for CO_2 in human blood, worked out in 1912 by Christiansen, Douglas, and myself. Thus the mixed arterial blood will, other things being equal, contain a normal proportion of CO_2, since the breathing will so regulate itself that the increased proportion of CO_2 in the arterial blood coming from the stagnant parts of the lungs will be just compensated by the diminished proportion in that coming from the over-

ventilated parts. In the case of oxygen, however, there will be no compensation, since almost no more oxygen than usual will be taken up in the over-ventilated parts, while in the stagnant parts the blood will be very incompletely oxygenated. This follows from the shape of the dissociation curve for oxygen in blood. The curves in question are reproduced in my recent book, "Organism and Environment," Yale University Press, 1917, where a short modern account of the physiology of breathing will be found. The necessary upshot is that the mixed arterial blood is imperfectly oxygenated, and symptoms of anoxæmia are produced. One result of this anoxæmia is that there is a slight increase in the breathing so that the average alveolar oxygen percentage is slightly raised, as was actually found. During muscular exertion the anoxæmia is of course much more marked, so that patients suffering from shallow breathing become dyspnœic and often blue in the face and dizzy. It is clear also that in the case of a patient suffering from restricted depth of breathing (an extremely common condition) an increase in depth will relieve the anoxæmia, as will, also, a slight addition of oxygen to the inspired air.

It is thus evident that the nervous disorder which produces shallow breathing may also produce serious symptoms of anoxæmia. The nervous disorder may be further specified as an exaggeration of the normal influence of the respiratory reflex discovered fifty years ago by Hering and Breuer. The Hering-Breuer reflex governs the depth of respiration, and its normal connection with the chemical regulation of breathing was investigated by Mavrogordato and myself in 1916. The causes of the exaggerated reflex are evidently so numerous that this symptom with all its consequences is a very common one in a great variety of illnesses. These causes include the various injuries, nervous shocks, and mental strains which produce "neurasthenic" or "shock" conditions, the toxic injuries in infections, anoxæmia itself (as for instance the anoxæmia of CO poisoning or poisoning by lung-irritant gases, or overstrain in heart affections) and irritation of the respiratory passages or lungs. We also found that shallow rapid breathing can easily be produced experimentally as a result of fatigue of the respiratory centre by excessive resistance to breathing, or of considerable shortage of oxygen continued for even a few minutes. Numerous cases were

also observed in which the shallow rapid breathing occurred in acute attacks, either during the night or by day. Attacks of angina pectoris, with their characteristic accompaniment of a vise-like feeling of constriction and inability to take in a proper breath, seem to be of this nature. Another notable fact discovered was that the anoxæmia from shallow breathing is far more easily produced in the recumbent position. This is evidently the key to the hitherto unexplained but very common symptom of orthopnœa.

The symptoms of anoxæmia met with in bronchitis, asthma, and emphysema can be explained on the same principle. When, owing to bronchial obstruction from swelling, presence of liquid, or constriction by the muscular coat, there is local hindrance to passage of air, the consequence is that parts of the lungs are imperfectly ventilated, with the same consequent anoxæmia as in the case of shallow breathing. Emphysema itself is caused by the excessive expansion of certain parts of a lung when other parts are unable to expand freely. The acute emphysema produced in this way in cases of chlorine poisoning was very striking; and evidently emphysema, when once established, will tend to the production of anoxæmia and hyperpnœa owing to the excessive ventilation of comparatively bloodless emphysematous parts of a lung, and correspondingly diminished ventilation of other parts. When the nervous disturbance which produces shallow breathing is superimposed on bronchitis, asthma, emphysema, or cardiac difficulties, acute anoxæmia must tend to be the result. In this connection it is essential to bear in mind that anoxæmia itself is a cause of the nervous disturbance, so that a vicious circle is produced which apparently accounts for many sudden deaths commonly attributed to primary cardiac failure.

In the light of the foregoing considerations it seems evident that there is a wide field for the therapeutic uses of oxygen; and probably oxygen will before long become one of the commonest of remedies. There are two ways in which it may be used; and the aims in using it must be distinctly kept in view in both cases. In the first place it may be given for a very short time with the sole object of breaking a vicious circle which has arisen temporarily. It has already been remarked that attacks of restricted depth of breathing often occur quite suddenly, for instance after influenza

or other infections, in broncho-pneumonia, in the course of heart affections, or of various nervous disturbances. In such cases the temporary administration of oxygen relieves the acute symptoms at once, and seems to cut short the attacks. As the symptoms are urgent the oxygen should be given freely and in the most direct manner. Perhaps the simplest method is to direct a very free stream of oxygen into the patient's open mouth. In the second place the oxygen may be required more or less continuously over a considerable period, with the object of preventing anoxæmia and all its very serious secondary effects on the nervous system, heart, and other organs, until time has been given for recovery from the primary source of danger. The treatment with continuous oxygen of a dangerous case of poisoning by a lung-irritant gas, or of a case of broncho-pneumonia accompanied by persistent anoxæmia, may serve as types of this method of using oxygen.

As regards actual procedure in administering oxygen, practical medicine has hitherto been greatly hampered in several ways. The steel cylinders in common use for containing oxygen are extremely heavy, in accordance with regulations made many years ago. Owing to the great progress of metallurgy it is now possible to make cylinders which are perfectly safe, but are so light that a cylinder containing 50 or 100 cu. ft. can be carried about with ease by a nurse. The war has shown how great is the necessity for these cylinders; and the restrictions on their use for ordinary medical purposes are now being removed. A second trouble has been the difficulty in manipulating and keeping in order the main valves for opening and closing the cylinders. Valves of greatly superior construction, and quite easily handled by anyone, are now available. It is essential for medical purposes that each cylinder, while in use, should be furnished with (*a*) a convenient pressure-gauge, so that it is always known how much oxygen is left in the cylinder; and (*b*) a reducing-valve which reduces the pressure to something easily controlled by a tap, and gives a steady pressure at all times till the cylinder is exhausted. A further requisite is a graduated tap, which can be set at any rate of flow desired. With a certain setting of the tap, at, say, 2 litres per minute, the same rate of flow is maintained for long periods. Thus with a quite light 50-foot cylinder 2 litres a minute can be maintained continuously for about twenty-

four hours. It is probable that in the immediate future it will be possible to use liquid oxygen in the same way, though there are still some technical difficulties to be solved. Under certain conditions liquid oxygen will be much cheaper than oxygen in cylinders, and may come to be an easily obtainable article of commerce.

For continuously administering oxygen in a simple and economical manner I devised an apparatus arranged as follows: An easily cleaned and disinfected metal face-piece with a pneumatic rubber rim fits lightly over the patient's mouth and nose. An opening on the front of this face-piece enables the patient to breathe air quite freely; but the opening is provided with a rubber flap which offers a very slight, but subjectively inappreciable, resistance to both inspiration and expiration. The oxygen enters the face-piece by another rather wide tube provided with a very lightly acting non-return valve, so that no oxygen or air can pass backwards. This tube comes from a small rubber bag with thin walls, and into this bag the continuous stream of oxygen from the cylinder is directed through narrow-bored but stout rubber tubing which cannot kink or collapse. On inspiration the bag is emptied, owing to the very slight suction caused by the resistance in the opening on the front of the face-piece. On expiration the non-return valve closes and oxygen again accumulates in the bag. In this way waste of oxygen during expiration is prevented, and by the movements of the bag it can be seen at once that the patient is getting the oxygen. If the face-piece is only loosely held over the patient's mouth this economy of oxygen will be lost, and at least twice as much oxygen will be needed. With a face-piece a certain amount of the patient's expired air is re-breathed, and this amount can be increased by blowing up the pneumatic rim. The CO_2 in the re-inspired air increases the depth of the patient's inspirations, but as the oxygen percentage in this air is very high this is usually entirely to the good, since the respirations become deeper, which helps in carrying air to all parts of the lungs. The whole of the apparatus just described is supplied by Messrs. Siebe Gorman & Co., London, whose co-operation in the experimental work required has been of great help.

The quantity of oxygen to be turned on must be decided by what is found necessary to obviate the signs or symptoms of anoxæmia. In some cases 1 litre a minute is sufficient, while in

acute gas cases as many as 4 litres have been required for a time in order to prevent cyanosis. Patients sleep quite comfortably with an apparatus on, and in those subject to dyspnœic attacks, and the accompanying terrifying dreams and fits of coughing, there is great advantage in the way of securing sound sleep. To patients who are actually suffering from anoxæmia, but are still conscious, the relief afforded is often very striking, as is also the effect in improving the heart's action; but where great anoxæmia has been present for some time, striking immediate improvement must not be expected, as has already been explained. The great object of treatment with oxygen should be to prevent anoxæmia and all its sudden dangers and direful after-effects.

Another method of administration, recently introduced by Mr. Bancroft and Dr. Hunt at Cambridge, is to keep the patient in an air-tight room containing air enriched with oxygen, the accumulation of CO_2 and moisture being prevented by a suitable purifier, and scrupulous precautions against fire being taken. This method presents certain evident advantages, and is practicable in hospitals where the requisite skilled supervision and funds are available.

CONGENITAL ARTERIO-VENOUS AND LYMPHATICO-VENOUS FISTULÆ. UNIQUE CLINICAL AND EXPERIMENTAL OBSERVATIONS

By William Stewart Halsted, M.D.

A. *Advance of a Proximal Arterial Dilatation Conformably to the Transposition, after Operation, of the Fistula.* Thanks to the assistance of highly competent secretaries I have abstracts of about 400 cases of arterio-venous fistula. These have been studied with especial reference to occasional observations on the dilatation of the arteries. In 52 instances proximal dilatation of the arterial trunk has been noted. I am quite sure that in almost every instance in which the fistula had existed for two or more months proximal dilatation of the artery would have been demonstrable if looked for.

Congenital arterio-venous fistula is rare, particularly so when unassociated with nævus. We have been able to find reports of only 2 cases without and 6 with nævus. Of the former neither was cured, unless we except the case of von Eiselsberg, in which an attempt to cure a fistula between the popliteal artery and vein was followed by gangrene, necessitating amputation of the thigh.

The following case, unique in several particulars, is reported to record the arterial changes observed at two operations, the second performed 6½ years after the first.

The patient, a girl æt. eleven years, was operated upon by the author, November 15, 1911, for a congenital arterio-venous fistula below the angle of the jaw on the right side. After the removal of a tumor-like mass of enormously dilated veins it was found that the fistula was between one of these and the external carotid artery near the bifurcation or ventricle of the common carotid. Fortunately a careful note was made at the operation of a very small, anomalous, ascending branch given off from the external carotid just proximal to the fistula (vid. Plate I). There was great dilatation of the common carotid and of the external carotid arteries proximal to the fistula, whereas the internal carotid was surprisingly small.

The vessels concerned in the fistula formation were excised, the aberrant artery happily being spared. The child was relieved of very distressing symptoms by the operation, but a few weeks later signs of a second, smaller fistula developed at a distal point, just below and in front of the ear. A second operation, proposed frequently, was not acceded to until last spring, $6^{1}/_{2}$ years after the first. At this operation, performed by my assistant, Dr. Mont Reid, in my presence, remarkably interesting observations were made. The tiny aberrant artery had become dilated almost to the size of a goose quill, and the internal carotid, which at the first operation was strikingly small, was, we estimated, as large as normal (vid. Plate II).

The explanation of the findings is, I think, clear. There were originally two fistulæ. The chief of these being eliminated at the first operation, the second, distal to the first, functioned more and more freely in the course of the 6½ years. The internal carotid, small at the first operation, being central to the main fistula, dilated after the subordinate or distal fistula became active; and the anomalous artery, also central to the main fistula, became dilated for the same reason. In regard to the development of congenital arterio-venous fistulæ Dr. Florence Sabin has kindly written me as follows:

"The anomaly of direct anastomoses between arteries and veins brings up an interesting point in the development of the vascular system, namely, that vessels which have served as arteries in the embryo may become veins and vice versa. One of the earliest examples of this occurs in the development of the vessels in the yolk sac of the chick. Primitively the anterior half of the yolk sac is entirely venous while the posterior half is entirely arterial, thus the omphalo-mesenteric vein and arteries are separated as far as possible by a wide capillary bed. Subsequently the omphalo-mesenteric arteries are accompanied by veins which develop as follows. As can be seen in Fig. 3, Plate 3, in Popoff's Atlas, (1) originally the omphalo-mesenteric arteries lie throughout their course in a capillary network. In the capillaries along the caudal border of the artery the blood flows away from the heart, while in those along its cephalic border it returns directly to the heart. As the chick develops, these two sets of capillaries along the main stem of the artery lose their connections with it and join each other, thus making a plexus which accompanies the artery and receives the blood which has passed out to the tip of the artery and returns it to the heart. In this plexus develops the vein which accompanies the artery. It is obvious that the retention of any of the original connections

of these capillaries with the artery would form the basis of a direct anastomosis between an artery and a vein.

"In connection with the development of the veins of the head and neck, it has been shown that the internal jugular vein develops in three

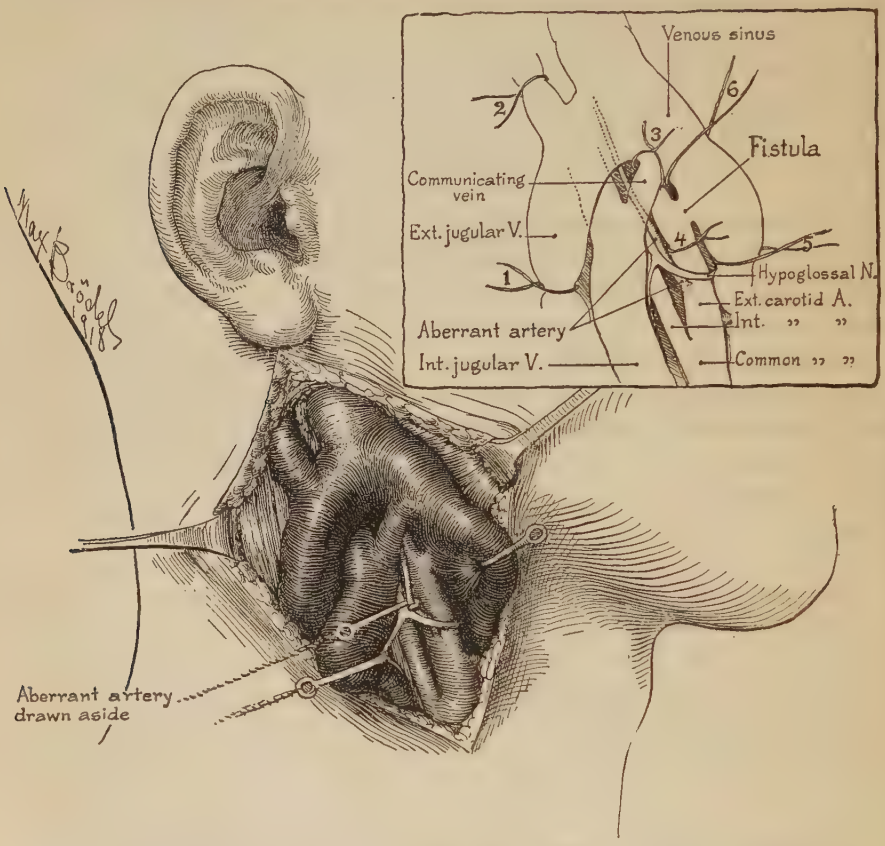

PLATE I. CONGENITAL FISTULA BETWEEN THE EXTERNAL CAROTID ARTERY AND A LARGE VEIN.

Appearances at the First Operation. Dilatation of the Common and External Carotid Arteries Central to the Fistula, and of the Venous Plexus. The Internal Carotid is Abnormally Small. There is a Tiny, Aberrant Branch of the External Carotid.

different segments. At first the blood of the cerebral veins, which make the first segment, passes through a long vein which rests on the hind-brain and ultimately becomes a plexus of vessels in the pia mater. From this deep vein the blood passes into the third segment, which is the anterior cardinal vein, and thence through the duct of Cuvier to the heart. This deep vein along the hind-brain is then eliminated from the drainage of the

cerebral veins by the development of a chain of capillaries between the aorta on the one hand and the cerebral veins and the anterior cardinal vein on the other. This chain of capillaries rapidly enlarges into the middle segment of the internal jugular vein. The original connections with the aorta are shown injected in Fig. 1, Plate 1, Sabin (1917) (2) for a pig embryo with 23 somites, measuring 7 mm. Moreover, injections of pig embryos measuring 14 or 15 mm. may still show slender connections between this middle segment of the internal jugular vein and the internal carotid artery.

"From these examples it is obvious that the details of the origin of each vessel should be worked out as a basis for specific anomalies that may occur in them, as has not yet been done for the external jugular vein, but the underlying principle that arteries and veins develop out of a common capillary plexus forms the basis for the persistence of direct connections between them."

B. *Enlargement of the Heart in Cases of Arterio-venous Fistula and Persistent Ductus Arteriosus.* A particularly interesting result of our clinical and experimental studies of arterio-venous fistula is the discovery that enlargement of the heart probably occurs after a time, as a rule, in the major cases. For ten years or more we have noted the condition of the heart in our patients with arterio-venous fistula and have, I believe, quite invariably found it enlarged—strikingly so in several instances. Dr. Mont Reid, of our Surgical Staff, has in preparation a report upon his experimental and clinical work on arterio-venous fistula in which he will offer convincing proof of our view that the fistula in its consequences may profoundly affect the heart as well as the veins and arteries. Skiagraphs show the effects of a fistula made 3½ years ago by Dr. Reid between the carotid artery and external jugular vein of a dog. The veins of the neck on both sides are dilated and the carotid artery is dilated central to the fistula. The heart after two years showed slight enlargement, and now, after three years, it has become pronouncedly increased in size. If the assumption is correct that the heart dilates in consequence of arterio-venous fistula, it is important that the fact should be brought to the attention not only of surgeons, but also of pathologists and internists, who evidently have overlooked it.

Our experimental and clinical observations on arterio-venous fistula and partial occlusion of large arteries may ultimately aid in the explanation of the sequelæ of certain congenital anomalies of

the heart and aorta. May we not regard the persistent ductus arteriosus as an arterio-venous fistula, the pulmonary artery and

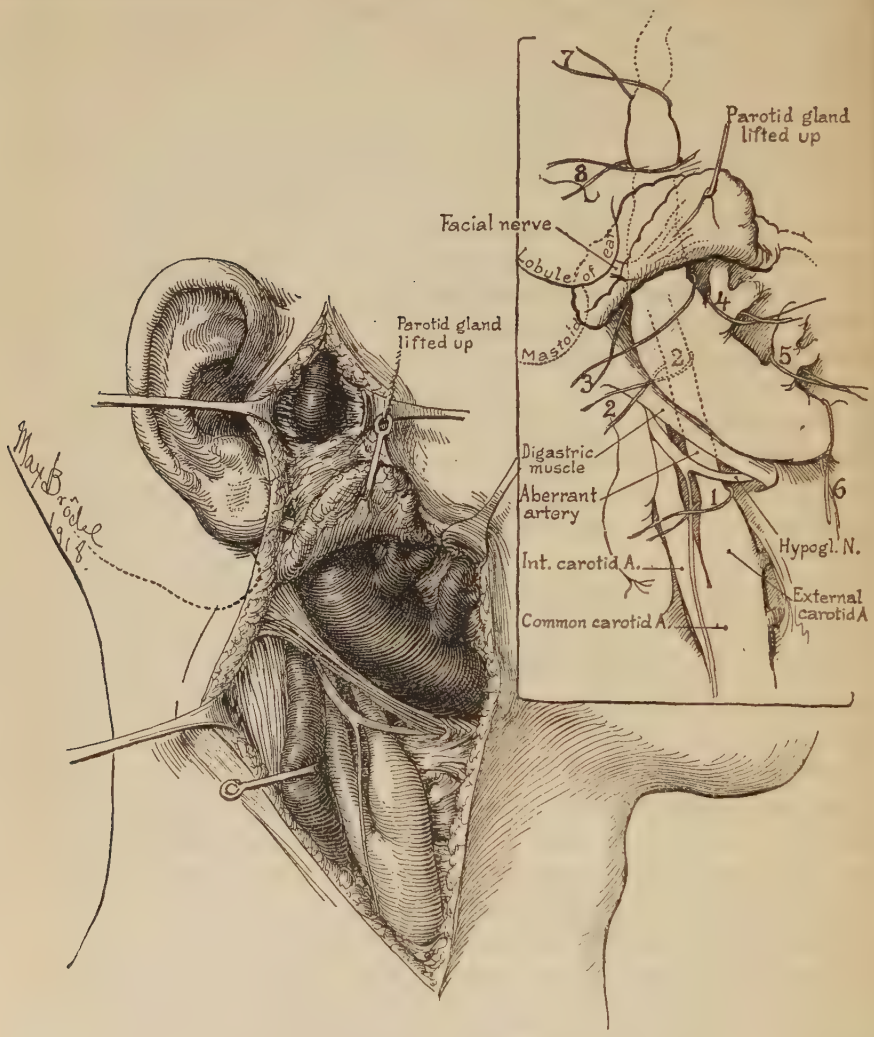

PLATE II. APPEARANCES AT THE SECOND OPERATION.

The Internal Carotid and the Aberrant Branch of the External Carotid Have Become Markedly Enlarged, the Fistula Having Shifted its Position to a Peripheral Point.

the right heart representing the venous side of the fistula? The enlargement of the left heart we might assume for the moment to be somewhat analogous to the dilatation of the artery proximal to a

fistula; and in the dilatation of the right heart and pulmonary artery we recall the dilatation of the veins.

My studies on the subject of the dilatation of an artery, which we find occurs distal to a constricting metal band and distal to the compression exercised by a cervical rib, have led me to investigate the results of the congenital coarctations of the aorta at or beyond its isthmus. I have been interested to find that in a large percentage of these cases of coarcted aorta there is dilatation, more or less delimited, beyond the site of the coarctation. The generally accepted view that this dilatation is to enable the aorta better to carry on the anastomotic circulation must, it seems to me, be erroneous. When we shall have ascertained more precisely the cause of the arterial dilatation obtained experimentally below constricting bands and of the dilatation of the artery proximal to an arterio-venous fistula, we may be able to explain the dilatation of the aorta beyond the congenital coarctation.

C. Plausible Explanation of the Presence of Blood in Lymph-cysts at the Second and Subsequent Tappings.

A few years ago, assisted by Dr. Heuer, I removed from the abdomen of a woman about forty years of age a huge congenital hygroma or lymph-cyst. The diaphragm was pushed high up into the right thorax and the liver was displaced far to the right and so rotated on its vertical axis that its inferior border, instead of being transverse, was parallel to and almost in line with the linea alba. The enucleation of the greater part of the cyst was easily accomplished, the few adhesions being disposed of by gentle, blunt dissection. Finally, when there remained only a few filamentous fibers binding the sac to the right adrenal gland[1] and the inferior vena cava, we proceeded with even more deliberation and caution. The adhesions to the vein were so delicate that the gentlest manipulation with the handle of the scalpel sufficed to break them. We had an unusually free and clear exposure of the vein and were operating without embarrassment. Suddenly blood gushed from a linear defect about 3 mm. long in the vena cava. The hemorrhage was promptly controlled and the slit in the vessel sutured. Proceeding thereafter with perhaps even greater delicacy, we were again confronted with a gush of blood from the vena cava at a higher point. Here we found a slit about 1.5 cm. long in this vein. The edges of the slit

[1] The relation of the cyst to the right adrenal gland was remarkable. In the course of stripping the sac's final delicate attachments we exposed a flat, black surface, evidently the spread-out medulla of the adrenal, about the size of a half dollar; parenchymatous oozing from this surface required for its arrest a few mattress sutures of fine silk.

were smooth, the linear defect being clearly not due to a tear or cut. The gap in the vein was closed by suture.

Dr. Heuer and I satisfactorily assured ourselves that there was no defect or special thinning of the wall of the cyst at the point contraposed to the larger of the two defects in the wall of the vena cava.[2]

The defects or slits were surely not artefacts. They represented, I believe, imperfectly closed embryonic communications between the vein and lymph buds or lymphatic vessels. Dr. Florence Sabin, to whom we owe so much for our knowledge of the origin and development of the lymphatic and vascular systems, writes me in regard to this case as follows:

"Recent work on the lymphatic system serves to demonstrate that lymphatic vessels are modified veins. It has been shown that lymphatic vessels occur first in the neck as sacs, lined with endothelium and packed with blood, which lie close to the jugular veins. The abdominal lymphatics begin as a sac which lies close to that part of the inferior vena cava which connects the two Wolffian bodies. Baetjer (3) showed in 1908 that in the pig this sac, which is the forerunner of the retroperitoneal lymphatics, communicates for a time with the inferior vena cava. These communications between the lymphatics and the abdominal veins, which are transitory in the pig, were then shown to be permanent in the South American monkeys by Silvester in 1912 (4) while in 1915 Job (5) demonstrated similar permanent connections in rodents. Thus the study of the development of the lymphatic system affords an explanation of anomalies involving connections between the lymphatic vessels and both the renal veins and the inferior vena cava" (6).

The statement has repeatedly been made that hygromata which at the first tapping have yielded a clear fluid may be found at all subsequent tappings to contain more or less blood. Only one explanation has been offered for the presence of the blood, viz., trauma of the wall of the cyst. This explanation has always seemed to me an unsatisfactory one, because the walls of these cysts are as a rule very thin and non-vascular. May it not, in view of the findings in our case, be possible that vestigia of lymphatico-venous communications (vid. Plates III and IV) are responsible for the admixture of blood which has occasionally been noted at only the second and

[2] The patient recovered promptly and has enjoyed excellent health since the operation.

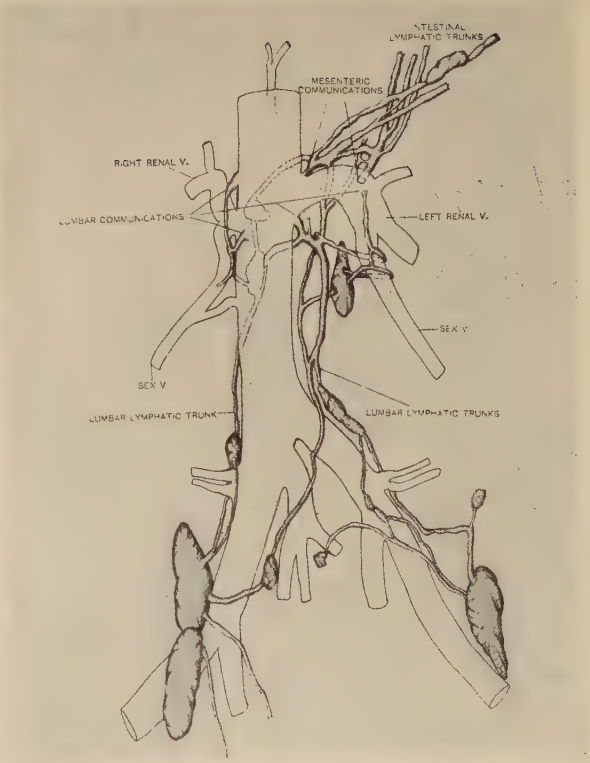

PLATE III. CEBUS HYPOLEUCUS, HUMB.
White-throated Capuchin.

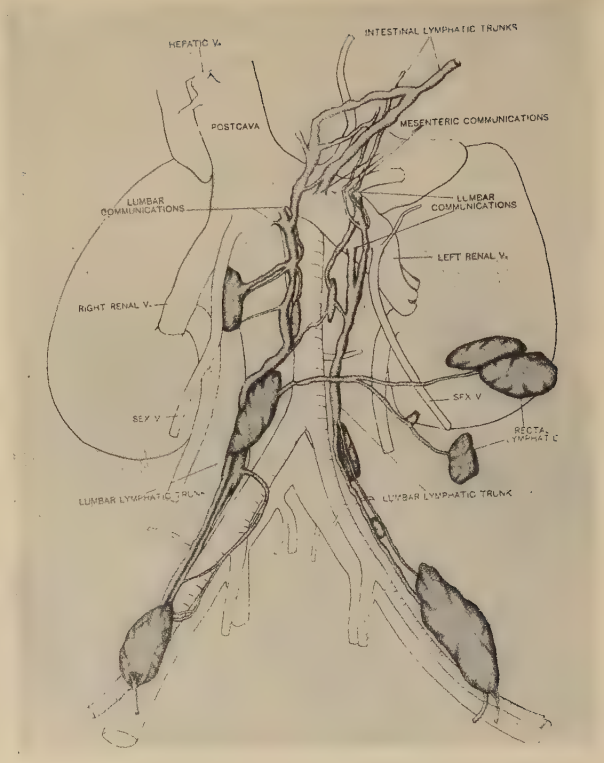

PLATE IV. ATELES VARIEGATUS, WAGNER.
Variegated Spider-monkey.

Reproduced from Charles F. Silvester's paper (l.c.) with the kind permission of the author and the editors of the *American Journal of Anatomy*.

subsequent tappings of lymph-cysts and is more frequently found at the first tapping? The negative pressure consequent upon the aspiration of fluid from the cyst might divert for the moment a little blood from the vein which had given origin to the hygroma's lymphatic bud or vessel. Thus the contents of the sac, clear at the first withdrawal, would be blood-stained at the second. Thereafter, with each tapping blood would be aspirated into the sac and hence clear fluid might never again be obtained.

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CLINICAL FEATURES OF ACUTE OBSTRUCTION OF THE CORONARY ARTERIES

By James B. Herrick, M.D., Chicago, Ill.

FOR several years practically the only clinical conception of obstruction of the coronary arteries was sudden death. This impression of the clinic was confirmed by Cohnheim, who, in his experiments, showed that dogs after ligation of any large branch of the coronary died in two minutes, and it was argued that it could hardly be otherwise, as the coronary arteries were end arteries, with only negligible non-functioning anastomoses. This unsavory reputation of the coronary arteries is only too well deserved, for in a large percentage of cases death soon follows the obstruction of any large branch.

But anatomists showed non-negligible anastomoses (1) by dissection, (2) by injecting one artery from the other, (3) by rendering the heart translucent and seeing the union between the right and left coronary, and (4) by skiagrams of the arteries after injection with such substances as bismuth or barium. Pathologists found many specimens where obstruction with resulting fibrosis had clearly been of long standing, thus showing the possibility of length of life after the accident. Experimenters like Porter, Miller, F. M. Smith, and others, have had dogs live even months after extensive ligation; and clinicians have observed cases where with ultimate autopsy control the patient has survived the accident by many days or months, often with a fair functional recovery.

A tentative grouping of the cases of coronary thrombosis based on clinical symptoms may be made:

1. Cases of instantaneous death, a group graphically described by Krehl, in which there is no death struggle; the heart beat and breathing stop at once.

2. Cases of death within a few minutes or a few hours after the obstruction. These are the cases that are found dead or clearly in the death agony by the physician who is hastily summoned.

3. Cases of severity in which, however, death is delayed for several hours, days, or months, or recovery occurs.

4. A group that may be assumed to exist embracing cases with mild symptoms, e.g., a slight precordial pain, ordinarily not recognized, due to obstruction in the smallest branches of the arteries.

It is Group 3 whose clinical phenomena are discussed, as illustrative of which three cases are briefly cited with necropsy findings.

Many of these points were treated with some detail in a paper written in 1912 (1). In that paper an attempt was made to picture the clinical feature of those cases in which death was not sudden. In subsequent papers by the author the same subject has been touched upon (2). But the condition is, I believe, more common than is generally supposed to be the case, and not infrequently lends itself to clinical recognition. It is for this reason that, in spite of having already written upon the topic, and in spite of the fact that there have been since 1912 occasional contributions from others dealing with the subject, I have felt warranted in emphasizing by repetition much of what I have already written. In response to the request of the editors the discussion will be brief.

Clinical Symptoms. Most of the patients are middle-aged or elderly men. The heart and blood vessels in many show the evidence of arterial and cardiac sclerosis; the blood pressure may be high. In others no sign of such change is to be made out. In fact, in two of my three cases with necropsy the only significant vascular sclerosis was in the coronary arteries; the hearts were of normal size and there had been no hypertension during life. In one there was slight involvement of the beginning of the aorta.

Previous attacks of angina pectoris may have been experienced. If this has been the case, the patient will describe the attack due to the coronary thrombosis as of unusual severity. Frequently there is no assignable cause for the attack, such as is commonly noted in the typical paroxysmal angina—walking, a heavy meal, undue excitement, etc.—though in some cases these factors seem to provoke the attack or, at least, greatly to aggravate it when it has started. The painful seizure is usually more enduring than in ordinary angina, the spell lasting many minutes or several hours, or a status anginosus developing. The location of the pain, as in the classical angina, is commonly substernal, with frequent radiation to the arms and neck. But in many of the thrombotic cases the pain is beneath the lower sternum or even in the upper epigastric region; and there may be no radiation to the arm or neck. This

epigastric reference of the pain, with the nausea and vomiting that frequently occur, often suggests to patient and physician some abdominal accident, such as acute pancreatitis, perforation of the gall bladder, or a gastric or duodenal ulcer (3). And these suspicions are strengthened by the fact that there are so frequently signs of shock and collapse—ashy hue of the face, clammy skin, and small, rapid, feeble pulse.

The heart is commonly rapid, even to 140 or more, though slow heart action has been recorded. There may be irregularities, such as tachycardia, extrasystoles, or partial block. The pulse usually lacks in strength and may be almost imperceptible, though in some cases the strength is wonderfully well preserved. Blood pressure is lowered, and tends to grow lower in the unfavorable cases. The heart tones may be startlingly faint, both because of the weakness of the heart's musculature and because of an acute emphysema that may develop and mask the heart sounds. Over the infarcted area a pericardial friction is sometimes heard. The heart may reveal evidence of dilatation by its increased area of dullness and its mitral systolic murmur due to relative insufficiency of the valve. Râles in the bronchi, with other evidence of pulmonary edema, may be present. Passive congestion of the kidney may show in a trace of albumin in the urine. In some cases within a few days cardiac edema of marked degree appears, the albumin being large in amount, the legs badly swollen, and free fluid being present in the abdominal cavity. The mind is commonly quite clear. I have been surprised at the preservation of bodily strength that is often manifested. Patients occasionally walk about within a few hours after such a seizure, and within a few days may be out of doors trying to attend to business.

These symptoms will often enable one to make a reasonably certain diagnosis of acute obstruction of the coronary artery. As in so many other conditions, the first essential is to think of obstruction as a possibility and to rid the mind of the notion that such a diagnosis is possible only at autopsy.

In the following three cases the diagnosis was confirmed by necropsy. In several in which no necropsy has been permitted or in which the patients are still living, diagnosis has seemed definite—as clear, for instance, as in most cases of obstruction of a cerebral vessel. I give very brief abstracts: Case I is reported more in detail in the article of six years ago; Case III with illustrations in *J. Am. M. Ass.*, February 8, 1919.

Case I. A man, aged fifty-five, was seized with severe pain low in the chest and epigastrium. He vomited. The physician, believing, as did the patient, that the attack was of gastric origin, washed out the stomach; but relief came only with morphine. The man lived fifty-two hours, re-

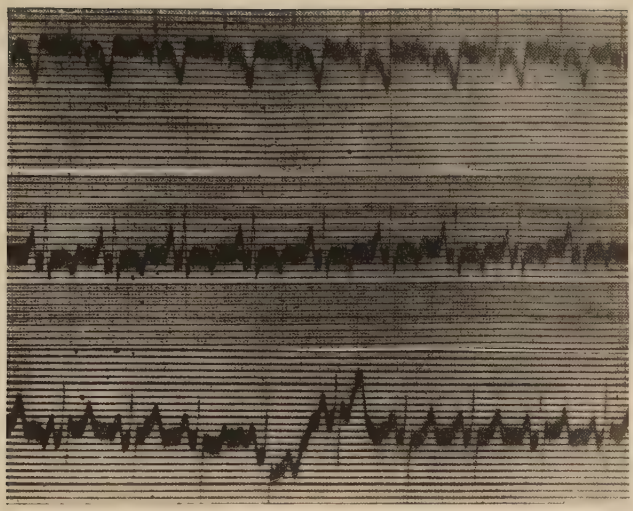

Fig. 1 (Case III). Electrocardiogram Taken May 3, 1917, Forty-one Days after the Coronary Obstructive Symptoms. Digitalis not Used at this Time.

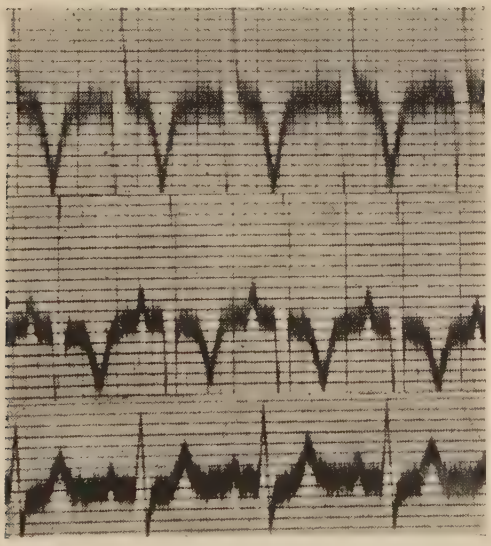

Fig. 2 (Dog). Electrocardiogram Taken Two Days after Ligation of Anterior and Posterior Descending Branches of the Left Circumflex Artery.

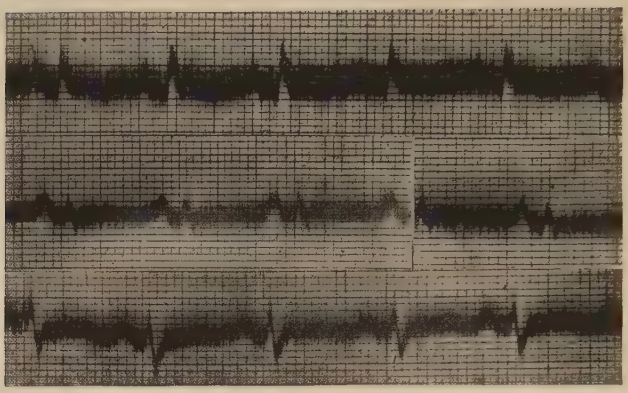

Fig. 3 (Case III). Electrocardiogram Taken September 27, 1917, 178 Days after Coronary Thrombosis.

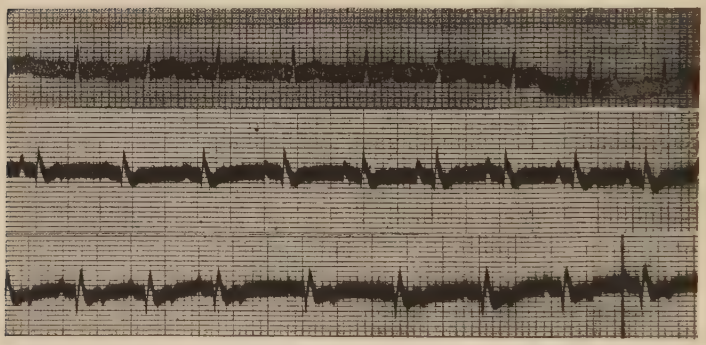

Fig. 4 (Dog). Electrocardiogram Taken Thirty-Four Days after the Ligation of the Ramus Circumflexus Sinister. Compare this Low-voltage Tracing with Fig. 3.

maining conscious to the last. His pulse from the first was rapid and very weak; heart tones nearly inaudible. An acute emphysema with many moist râles developed. No abdominal or other than cardiac cause could be made out as an explanation of the condition. The temperature never was above 99.2° F. The left ramus descendens was found plugged by a thrombus at a narrow spot where there was a small pathological mural roughening and thickening.

Case II. A man aged sixty-two, while walking on the board walk at Atlantic City, was seized with a terribly severe pain in the lower precordia. He was helped to the hotel, but refused to call a physician while in Atlantic City or for the next two days while in New York, for, as he said, he knew from the severity of the initial pain, the great weakness and difficult breathing, that he would be ordered to a hospital, and he wished to get to his home in Chicago for his illness and, as he feared, his death. He lived over two weeks from the onset of the attack. His heart when he reached Chicago was dilated, weak, and somewhat rapid. His blood pressure became progressively lower. There were dyspnea, cyanosis, marked edema of the legs, and albuminuria. Death was as in ordinary cardiac failure. Necropsy revealed recent plugging by a thrombus of the descending branch of the left coronary, with softening of the heart muscle at the left apex and the lower interventricular septum.

In this, as in the other case, the aorta was free from evidence of sclerotic change. No other vascular lesions were found than the isolated patches of sclerosis in the coronary. It happened also that in each case the patient had only a short time before been carefully examined by competent physicians and had been pronounced in good health as to heart, blood vessels, urine, etc.

Case III. A physician, aged forty-two, who had never suffered from angina pectoris, had no acute or chronic infection so far as he knew, and who regarded himself as free from cardiovascular and renal disease, was seized while in this seemingly good health, with a sudden, excruciating pain in the lower sternal region, which pain radiated to the arms and to the epigastrium. He was profoundly shocked, very weak, and nauseated, the skin cold and clammy, the pulse rapid and thready. His colleagues who saw him thought he would die in a very short time. Morphine was necessary to control the pain. In ten days he was able to be about and even tried to do some professional work. But in a few days his weakness, precordial distress on exertion, dyspnea, and irregular, rapid, and small pulse, caused him to give up. A little later my office assistants ventured a diagnosis of coronary obstruction, a diagnosis that I felt was correct when I saw him a few days afterward. Electrocardiograms taken on these two occasions

gave support to these opinions. Rest and small doses of digitalis were ordered, and improvement followed. The summer vacation was spent on an island, where there was considerable violation of the injunction as to quiet and digitalis, with occasional dyspnea and cardiac irregularity as warning that the heart was not normal. He contracted an infectious bronchitis and hastened to Chicago, where, in a deplorable condition, he went under my care in the Presbyterian Hospital, September 26, 1917, dying of a pneumonia twelve days later, October 8, 1917, five months from the time of his initial attack of pain.

The heart was large, the left ventricle at the apex, the lower interventricular septum and the papillary muscles, especially the anterior one, thinned, scarred, and cutting like gristle. The descending branch of the left coronary and the large descending branch of the left circumflex were completely obliterated by old thrombi. The only sclerotic changes in the arteries were a few small patches in the aorta close to the openings of the coronary arteries, and similar patches in the coronaries themselves. It may be added that no history or stigmata of syphilis were noted during life, and that the Wassermann test on the blood had been negative.

Experimental Work. I wish to call attention briefly to certain experimental work that has a direct bearing on the question of obstruction of the coronary arteries. Dr. Fred M. Smith, (4) in the Presbyterian Hospital and Rush Medical College, studied experimentally the coronary arteries in dogs.

Method. He took an electrocardiogram of each dog when under ether. Then the desired branch of the coronary artery was ligated. Following the operation electrocardiograms were taken at intervals varying from a few minutes to many days or weeks. On all dogs that died or that were killed a post-mortem was made, and the gross and microscopic structure of the myocardial lesion was studied. Electrocardiograms were compared to see if there was uniformity in the tracings made after ligation of the same arteries and with the same lesions. Lastly, in human beings with symptoms suggestive of coronary thrombosis, the electrocardiograms were compared with those in dogs.

Results. 1. Dogs may live for months or may recover after ligation of branches of the coronary arteries, even branches of considerable size. This is contrary to the findings of Cohnheim, but is in accord with those of Porter Miller and others.

2. After the ligation of special branches the lesions produced in the muscle are fairly constant as to location. These lesions are most marked in the endocardial and subendocardial tissues, that is, in the conducting region, a point brought out by Oppenheimer and Rothschild.

3. Following the ligation numerous irregularities, such as extrasystoles, tachycardia, auricular fibrillation, auricular flutter, and ventricular fibrillation, may result. Thus far it has been impossible to predict the type of irregularity that will follow a ligation.

4. There seems to be a fairly constant variation in the electrocardiogram following the ligation of a particular branch of the coronary.

5. There is some hope that the work may assist in interpreting abnormal human electrocardiograms. The thought has been that if it can be proved that with a certain artery obstructed there is a definite lesion in the heart muscle or in the conducting system, and if with that lesion there is a definite electrocardiogram, may we not, when we encounter that abnormal electrocardiogram in the human being, particularly if he has had symptoms suggestive of coronary thrombosis, be able to state with a reasonable degree of certainty that the patient has had obstruction in a particular portion of the coronary system? May it perhaps be possible to localize a lesion in the coronary system with an accuracy comparable to that with which we locate obstructive lesions in the cerebral arteries?

This work needs confirmation as to the regularity of the results obtained, and especially as to the interpretations and conclusions. Confirmation from necropsies is particularly desired. Patients with this condition do not present themselves very often. A large proportion with coronary obstruction die a sudden death, or are too ill to come to the office or to a hospital where electrocardiographic tracings can be taken. And yet we have been able to take several suggestive tracings in patients in whom we believe these coronary thromboses have occurred; and in one of the cases, Case III, in which the patient lived five months after obstruction, the abnormal electrocardiograms gave helpful confirmatory evidence. Necropsy revealed the lesions anticipated.

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THE CLINICAL ASPECTS OF THE PNEUMONIA OF INFLUENZA

By C. P. Howard, M.D., Iowa City, Iowa

Professor of Theory and Practice of Medicine, State University of Iowa

THE material for the following observations consisted of 125 cases of pneumonia occurring among 1100 cases of epidemic influenza among the S. A. T. C. and the nursing and medical staffs of the University Hospital, as well as some 25 pneumonia cases seen in consultation in the State.

All are agreed that the pneumonia of the present as well as of previous epidemics of influenza presents many unusual features. Whether these peculiarities are due to an infection with some special micro-organism as the *B. Influenzæ*, or even to some hitherto unrecognized virus, or merely due to the more common secondary invaders, the streptococcus and the pneumococcus, is of course a moot question. Personally we have lost faith in the Pfeiffer bacillus as the exciting factor in either the influenza itself or the secondary pneumonia that occurs in at least 10 per cent of the cases. In Iowa, as in the vast majority of States in this country and practically universally in Europe, the *B. Influenzæ* was chiefly remarkable for its absence—at the most being found in only 25 per cent of cases. (1) Perfection of technique cannot explain an incidence of from 82 per cent to 100 per cent in Massachusetts (2) and New York (3), while in Iowa, our clinical bacteriologist, Dr. Frieda Hirschberg, failed to isolate it from the nasopharynx, sputum, blood stream, and pleural exudates. At autopsy it was found only once or twice in direct cultures from the lungs.

No definitely proved pathogenic organism offers such an analogy. We are therefore more inclined to regard the virus of influenza to be as yet undiscovered, and to assign the etiological rôle of the pneumonia to a secondary invasion by the various pneumococci and the *Streptococcus hæmolyticus* and *viridans*. For this we have an analogy in measles, pertussis, and to less extent scarlet fever.

Clinically it is difficult to distinguish the lobar from the lobular type. In our experience the vast majority of cases were atypical lobar cases. The post-mortem table reveals the fact that the majority of these cases are actually confluent broncho-pneumonias to which we will apply the name "pseudolobar."

I. *Pseudolobar Pneumonia.* Rarely does the pneumonia appear before the third or fourth day of the disease. In an occasional fulminating case well-defined symptoms and signs of the pneumonia may be present from the end of the first day. On the other hand, occasionally the symptoms may not appear until two or more days after the influenza has subsided. In the average case some time between the third and the fifth days the temperature rises to 104° or 105° F., usually without chill or at the most chilliness, and the patient becomes more toxic and often delirious. Pain in the chest is relatively rare and in our experience not as frequent as pain referred to the abdomen. This is, of course, due to the rarity of early fibrinous pleurisy and to its appearance when present on the diaphragmatic-pulmonary pleura as frequently as on the costal-pulmonary layers. Dyspnea and increase in the respiratory rate are strikingly absent except in the terminal stage of the disease. In fact only careful observation will detect slight movement of the alæ nasi with respirations between 24 and 28 per minute.

The pulse rate, too, is relatively little disturbed and in proportion either to the height of the fever, the degree of toxemia, or the extent of lung involvement. Here, again, it is not until a few hours before death that the pulse rises above 100, and many charts show lower rates recorded eight or even four hours before death. The blood pressure, as well as pulse pressure, further show the slight disturbance of the circulatory apparatus. On the other hand, cyanosis soon manifests itself either as a deepening of the febrile flush or, especially in the severe cases, as a well-defined bluish discoloration of the lips, ears, and finger tips, together with a grayish waxy tint of the entire surface of the body.

Herpes is exceedingly rare, though more apt to occur in the case developing in convalescence with chill and the other more typical symptoms of pneumonia.

Synchronous with the appearance of the cyanosis the patient becomes unusually restless and apprehensive, suggesting often the

coma vigil of the final hours of a peritonitis case. Nausea and vomiting may now make their appearance, followed very shortly by the other signs of acidosis, namely, a sweetish odor to the breath, a dry, harsh skin, and the presence of both acetone and diacetic acid in the urine. Whether this acidosis results directly from the infection or is due to the gastric irritation and the consequent vomiting, so common in the severe cases of influenza, we are unable to decide from the available data, though we are inclined to regard it as an expression of a bacterial acidosis.

The cough, which was at the beginning of the influenza more or less troublesome and of a paroxysmal almost whooping cough variety, becomes more frequent and is now associated with a mucoid tenacious sputum containing varying amounts of blood. While in many the sputum is merely blood stained and of a more or less typical rusty variety, we have been impressed with the frequency in which a free hemoptysis has occurred; in fact it is not uncommon to see 6 to 12 ounces of bright red blood coughed up in as many minutes. This must be due rather to the intense engorgement of the bronchial mucosa than to a rapid congestion of the affected pulmonary tissue, for it was noted more frequently in the cases in which the epistaxis was most marked.

Incidentally in no disease, typhoid fever not excepted, has an epistaxis been so frequent and so profuse and persistent. When severe it usually prognosticated a serious if not a fatal clinical course.

The leucopenia of the initial influenza was found to persist throughout the course of the disease, especially in the severe fulminating cases. In the more favorable and less intense infection 12,000 to 15,000 white cells per cu. mm. were commonly found late in the disease. It was only in the occasional pneumonia of convalescence that higher counts (20,000) were noted.

The physical signs are of great interest and appear so rapidly that an examination of the chest at twelve-hour intervals should be a routine procedure.

In spite of the harassing cough and substernal soreness that exist in the first three days of the influenza, the physical signs in the chest are practically *nil*, with the exception of an occasional sibilant râle over the larger bronchi. About the third or fourth day, often before there are suggestive symptoms of a pneumonia, there

can be heard over the lower lobes, particularly in the interscapular region, peculiar sticky, moist, râles, differing from the fine crepitant râle of the ordinary pneumonic infiltration, and resembling more the medium moist râles of pulmonary edema than of any other condition that we can recall. The other auscultatory phenomena are at first usually entirely absent, though occasionally there is either some enfeeblement of the respiratory murmur or more rarely some harshness of the breath sounds, suggestive of the broncho-vesicular type of breathing. Certainly no change can be detected at this stage in the transmission of the spoken or whispered voice sounds.

Further, even the most careful percussion will fail to yield any definite change in the note in the first few hours. Then suddenly at the end of twelve to twenty-four hours there will appear over one or other interscapular region, more commonly, perhaps, the left, an area of hyper-resonance, almost of tympany, followed shortly by impairment or even frank dullness. By the time dullness has appeared there can be heard distant or even loud bronchial breathing together with the fine crepitant râle usually heard in pneumonia. At the same time bronchophony and pectoriloquy often can be detected. Increase in tactile fremitus seems to be the exception; more commonly have we noted diminution of the vocal fremitus throughout the course of the disease.

By the time that the majority of the above signs can be detected over one interscapular region, involvement of the opposite lower lobe or more rarely of an upper lobe is evident. At least in a considerable number of cases hyper-resonance and harsh vesicular breathing with the peculiar type of râle can be detected over the upper lobes, particularly posteriorly. By the third or fourth day in the severe pneumonia there develops a striking pulmonary edema, which seems to overwhelm the patient in the course of a few hours. One of the many interesting peculiarities of this edema was that it was never associated with evidence of dilatation of the right ventricle, as determined at least by percussion. In fact we have been at a loss whether to assign the mode of death to this pulmonary edema or to a toxic effect on the respiratory center in the medulla.

At least we can say the cause of death is more often respiratory than cardiac in the influenzal pneumonia. From my notes of some

fifty fatal cases there were only two cardiac deaths, one in a man of fifty in whom cardiac sclerosis and diabetes had been present for two years, and the other in a lad of nineteen who died suddenly on the seventh day of convalescence from an acute myocarditis with dilatation.

A good deal has been written about the value of the *x*-ray in detecting this type of pneumonia. (4) We can only say that the skiagram is no doubt another physical sign, but of no earlier appearance than the others, and certainly of no more diagnostic value except in the rare slowly developing central pneumonia. To test its value one morning we personally made careful notes on twelve cases in the early stages of the disease, and in only one, which was skiagraphed six hours after the physical examination was made, was a pneumonic patch detected in the opposite lobe which had not been found by ordinary physical methods. For purposes of graphic record, as well as in cases of doubt between a massive consolidation and a pleural effusion, it is of unquestionable value. However, in the latter case the exploratory needle is much more reliable.

The *course* of the disease varies considerably. If death does not occur by the fourth or fifth day there is an increasing chance of the symptoms abating by lysis or even in some cases by crisis on the seventh to the fourteenth day. The consolidation is very slow to resolve, and never before have we seen so many cases of delayed resolution as in this epidemic. In fact, it is not uncommon to find dullness and suppressed breathing two weeks after the temperature has reached normal. In several cases the signs at the base have persisted for two or three months, leading to the natural suspicion of an empyema and consequently to exploratory aspiration. It is, of course, in these cases that the skiagram is of distinct value, and yet we can only recall one case, and that in a child of four, in which the ordinary physical signs and the septic type of the fever suggested an empyema, while the skiagram pointed to a pneumonia, which was confirmed by the negative exploratory puncture and later by the complete disappearance of both symptoms and signs without drainage of the pleura. This delay in resolution in the upper lobe may suggest of course the development of a tuberculous process, a suspicion which is, alas, sometimes later confirmed. This slowness in resolution was seen on several occasions post-mortem, and can

be readily explained by the greater connective tissue development in one type at least of this pneumonia.

While in some States *empyema* has been said to be rare, this has not been our experience in Iowa, where we have had it complicating 10 per cent of our cases. This is, of course, not such a high incidence as occurred in the winter and spring of 1918 in the streptococcic pneumonia, but nevertheless there were in both groups a similar flora (pneumococcus and *Streptococcus hæmolyticus*), an appearance early in the pneumonia, a severe systemic infection, and a tendency to pocketing of the pus.

Even in the influenza epidemic it was quite common to detect it before the temperature had reached normal and when the signs of a frank consolidation existed in the opposite lung. For this and other reasons we are inclined to believe that in Iowa, at least, the pneumonia of this influenza epidemic is due to the same secondary invader that was present last year, and that possibly even an increase in the distribution of a highly virulent type of pneumococcus and streptococcus is responsible for the widespread nature of the so-called epidemic influenza.

II. *The Broncho-pneumonia.* A true broncho-pneumonia at least clinically was distinctly rare. It occurred in two groups of cases. In one, of an exceedingly mild nature, there would appear for a day or two increase in the cough, some bloody or rusty sputum, slight cyanosis and dyspnea, and over the upper portion of the lower lobes and posterior aspects of the upper harsh breathing and fine moist râles. No sign of consolidation would be detected and the patient would make an uninterrupted recovery.

In another group the patient would be critically ill from the beginning of the influenza and would early have cough, bloody sputum, cyanosis, delirium, and high fever, but apart from harsh breathing and fine râles no sign of a pneumonia. Death would close the scene on the fourth or fifth day and autopsy would reveal a broncho-pneumonia of considerable extent, but too early to have coalesced into recognizable areas of consolidation. These, no doubt, are the cases regarded by some as more truly characteristic of influenza, and from which many have isolated the bacillus of Pfeiffer in pure culture.

Treatment. Nothing that we have done therapeutically has

seemed to be of any material assistance to our patients except the usual symptomatic treatment, including the free use of whisky, strychnia, camphor, and digitalis almost from the first appearance of the pneumonia. Following the suggestion of Litchfield (5) we tried the intravenous administration of glucose (25 per cent) solution in all severe cases with no striking effect, certainly no more than would encourage its further trial. Rushed as we were at the height of the epidemic, many cases received 300 to 450 c.c. of glucose at twelve to twenty-four hour intervals, for two, three or even more doses; but a survey of these cases leaves me at least non-enthusiastic.

In only some five or six patients was convalescent serum (6) used, but with such equivocal result that it was given up. As not one of our typed cases yielded a type I pneumococcus we did not use any of the anti-pneumococcus serum.

As far as vaccine therapy was concerned we did not deem it as worthy of trial, as we do not approve of the administration of the mixed vaccine in any disease, and we regarded the saline or lipo-vaccine made from *B. Influenzæ* as non-specific for our group of cases at least.

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IDIOPATHIC HYPERTROPHY OF THE HEART IN YOUNG CHILDREN

By John Howland, M.D., Baltimore, Md.

(From the Harriet Lane Home of the Johns Hopkins Hospital and the Department of Pediatrics, Johns Hopkins University)

THE following is a description of the clinical symptoms and the autopsy findings in the cases of five young children who died in the Harriet Lane Home with great hypertrophy of the heart, which could not be explained upon anatomical grounds:

Case I. S. C., white, age 2½ years, No. 11,618. The mother of the child was not vigorous. She complained of "heart trouble." The child was the elder of two, the other being six months old and well. Patient was born spontaneously at term and was nursed for five months, began to walk at ten months, and talked at a year and a half. Had mild pertussis in March, 1916, later complaining of pain in the region of the heart. Had "fainting spells" lasting for perhaps ten minutes at a time. Her appetite became poor and at times she was cyanotic. In July, 1916, she was brought to the hospital on account of increasing attacks and occasional cyanosis.

Physical examination showed a child moderately well nourished with slight cyanosis of nose and ears. Lungs clear, precordium slightly prominent. There was a strong cardiac impulse, and it could be plainly made out that the heart was greatly increased in size, chiefly to the left. The left border was 7 cm. to the left of the mid-sternal line in the fourth interspace and 9 cm. to the left in the fifth interspace. Both sounds were clear at the apex; at the base there was a short systolic murmur, heard best in the third left interspace, transmitted a short distance upward, but not into the vessels of the neck. The liver could be felt just below the costal margin. The spleen could not be palpated. White blood cells, 14,800. The child improved in the hospital. The temperature was always normal. The heart remained of the same size, but the systolic murmur disappeared. The color became better and she was discharged at the end of ten days. Fig. 1 is a copy of the *x*-ray made just before discharge. In August the attacks of cyanosis returned and were very severe, particularly interfering with the child's rest at night. In September she was admitted to another hospital, hence the his-

tory is fragmentary. She had suddenly developed difficulty with the use of her right side, which was believed to be the result of a cerebral embolus. She had no fever, but the dyspnea and cyanosis increased, and on September 28th the respiratory distress rapidly increased and she died on this day.

Autopsy by Dr. Burrows. The body is that of a well-nourished child. It measures 89 cm. in length. There is a considerable amount of subcutaneous fat. The peritoneal cavity is smooth and glistening, and contains a few c.c. of clear straw-colored fluid. The pleural and pericardial cavities are smooth and glistening and contain a few c.c. of fluid. The mesenteric and retroperitoneal glands are large, firm in consistency, grayish and pink in color. The *thymus* is small and weighs *9 gms.*

The heart is enlarged and displaced to the left. The pericardium is smooth, moist, and glistening. The pulmonary and systemic vessels are filled with fresh post-mortem clots. *Weight 120 gms.* (Average for this age: Bovaird and Nicoll (1) 58 gms., Verordt (2) 59 gms.) The measurements are as follows:

Pulmonary valve	5 cm.
Tricuspid valve	7 cm.
Mitral valve	5 cm.
Aortic valve	3.5 cm.
Aorta	3.5 cm.
Left ventricular wall	6 mm.
Right ventricular wall	6.6 mm.

The right heart is greatly hypertrophied and dilated. Its internal chamber is beautifully trabeculated. The pulmonary artery is dilated. The valves are thin and delicate and appear to be competent. The right auricle, slightly dilated, shows no evident thickening of its walls, while the left auricle and left ventricle appear normal in size. The coronary arteries appear normal. The aortic and tricuspid valves are thin and delicate and appear competent. Epicardium smooth. Aside from the hypertrophy of the right ventricle, the myocardium shows nothing unusual.

Lungs: Right lung weighs 125 gms.; left, 120 gms. The walls of the larger vessels are thin and delicate. The bronchial mucous membrane is roughened, deeply injected and covered with a layer of mucus. The cut surface is smooth and moist. The peribronchial glands are small and pink in color.

The spleen weighs 38 gms. It measures 8 x 4 x 3 cm. The capsule is smooth and translucent. The organ is very firm. The Malpighian corpuscles are numerous, sharply circumscribed from a deep red pulp.

The liver weighs 420 gms. It measures 17 x 12 x 4 cm. The capsule is

smooth, thin, and translucent. The cut surface has a grayish-yellow color. The central veins stand out prominently. The lobules are very easily seen.

Gall bladder: The walls are thick and edematous. The mucous membrane is of a deep yellowish-brown color. The gall bladder is filled with a yellowish-brown, rather thick bile.

Stomach and intestines: The mucous membrane shows post-mortem change. Bile flows readily from the papilla of Vater. Throughout the entire intestines the solitary nodules and Peyer's patches are very much enlarged and deep gray in color. The intestines are injected throughout their entire course. There is no evident ulceration.

The pancreas weighs 35 grams and shows nothing unusual.

The adrenals appear normal.

The kidneys are very firm. The capsules are thin and strip easily over a surface on which the stellate veins stand out plainly. The right kidney weighs 44 gms. and measures 6.5 x 4.25 x 2.25 cm. The left weighs 38 gms. and measures 6.5 x 3.5 x 2.25 cm. The medulla of the kidneys is deeply injected and is sharply circumscribed from the grayish cortex. The cortex measures 5 mm. in thickness.

The ureters, bladder and genitalia appear normal.

The aorta appears normal.

Neck organs: The trachea and laryngeal mucous membranes are deeply injected and roughened. The thyroid shows nothing unusual.

The brain and spinal cord shows nothing abnormal.

Case II. G. S., white, age sixteen months, No. 9885. One of twins. The other child died at the age of three months. Weight at birth 4 pounds 2 ounces. Artificially fed from birth with much difficulty. Admitted to the hospital at the age of three months, a very poorly nourished child, weighing 5 pounds. She vomited repeatedly and lost weight to 4 pounds. It was then found that the regurgitation was the result of rumination, and she was fed a mixture of thick cereal and milk. Thereafter she gained rapidly and was discharged from the hospital weighing 8 pounds 3 ounces. At home she continued to do well and at the age of fifteen months weighed 16 pounds. On January 18, 1917, marked respiratory distress began and continued almost uninterruptedly thereafter. At no time was the temperature above 100° F. Her appetite became capricious. This continued for a month; then she was admitted to the hospital. She was a short but plump child, pale, irritable, breathing with marked difficulty. Physical examination of the lungs was negative. There were no râles. The heart was much enlarged. The apex beat was in the fifth space outside of the nipple line. The sounds were feeble. Dullness extended from the anterior axillary line on the left side to 3 cm. to the right of the mid-sternal line in the fourth interspace. Fig. 2

is a copy of an *x*-ray made a few days before death. White blood cells 8700. Red cells 3,340,000. Hemoglobin 40 per cent. Pirquet test negative. The dyspnea increased, the chest became full of moist râles and on February 19th the temperature rose sharply. There were evidences of edema of the lungs, and the child suddenly died, without, however, any marked cyanosis.

Autopsy by Dr. Clark. The body is that of a well-nourished white female infant, 54 cm. in length. The thorax is slightly asymmetrical, the left side appearing slightly more bulging than the right. The costochondral junctions are not enlarged, and the epiphyses of all the long bones have their usual relative size and proportion. The serous surface of the peritoneal cavity is quite smooth and glistening, and the peritoneal cavity contains no excess of fluid. The liver extends three fingers' breadths below the costal margin in the right mammary line. On removing the sternum the lungs collapse moderately. The left lung is displaced upward by the heart, which is greatly enlarged, and the lung occupies only a small area at the upper portion of the chest. The greater part of the left chest is filled by this large heart. The right pleural space is free of adhesions, the serous surfaces are smooth and glistening, as are also the serous surfaces of the left pleural space, and neither pleural space contains any fluid. The pericardial membranes are smooth, and the pericardial cavity contains about 2–3 c.c. of slightly blood stained fluid.

Thymus: In the upper anterior mediastinum there is a thymus gland which weighs *12 gms.*

Heart: As noted above, it extends practically over to the left chest wall, displacing the left lung upward. The pericardial membranes are smooth and glistening, and the heart in its general outline shows nothing unusual. The pulmonary artery is opened *in situ*, and the orifice of the ductus Botalli is found to be occluded; the ductus Botalli is entirely closed. It is represented by only a small band of fibrous tissue which extends between the pulmonary artery and the arch of the aorta. The pulmonary artery contains no thrombi. The right auricle is somewhat dilated. The leaflets of the tricuspid valve are delicate, translucent, and show no evidence of inflammatory change of any kind. The chambers of the right ventricle are also dilated and the walls are rather thin because of this. Otherwise nothing unusual is to be noted in the cavity of the ventricle. The leaflets of the pulmonary valve show nothing unusual. The endocardium throughout is delicate. The leaflets of the mitral valve are exceedingly delicate and show no vegetations or change of any kind. The cavity of the left ventricle also is dilated, which gives the wall a thin appearance. The leaflets of the aortic valve show nothing unusual. All of the valve ori-

fices of the heart have about their usual proportion and present no evidence of stenosis or obstruction of any kind. The foramen ovale shows a small opening which is covered by a flap of tissue, so that one would interpret it as being an anatomical rather than a functional patency. The coronary arteries show nothing unusual. The heart weighs *180 gms.* (The average for this age according to Bovaird and Nicoll (1) is 37 gms., and according to Vierordt (2) *45* gms.) The measurements are as follows:

Tricuspid ring	*5.5* cm.
Aortic ring	2.*5* cm.
Pulmonary ring	3.0 cm.
Mitral ring	4.*5* cm.
Left ventricular wall	6.0 mm.
Right ventricular wall	1.0 mm.

Lungs: The pleural surfaces are smooth and glistening. The lungs are moderately collapsed. The lung substance through the pleural surfaces has the usual pale pink color with slightly increased red color in the dependent parts. On palpation both lungs are crepitant. On section the lungs show a surface from which there is a slight excess of frothy fluid exuding, but the cut surface is quite uniform in appearance. In the dependent parts there is a moderate degree of hypostatic congestion apparent. Dissection of the bronchi and branches of the pulmonary artery shows nothing unusual. The bronchial mucosa is quite delicate. The trachea and bronchi are more or less filled with a frothy serous fluid. The vessels contain no thrombi.

Spleen: The capsule is smooth and glistening and through it the Malpighian bodies stand out quite distinctly. The cut section appears normal. The spleen weighs 22 gms. and measures 6.*5* x 3.*5* x 1.*5* cm.

The pancreas weighs 13 gms., is 9 cm. in length and appears normal.

Stomach and intestines appear normal.

The liver occupies its usual position and has about the usual relative size, shape, appearance, and consistency for a child of this age. The capsule is smooth and glistening. The cut section is quite uniform and rather yellowish in appearance. The bile ducts and blood vessels show nothing unusual. No areas of unusual change are to be seen within the liver substance. The liver weighs 300 gms. and measures 14.*5* x 8 x 4 cm. The gall bladder appears normal. The mucosa is delicate and the bile within the gall bladder is clear and yellow.

Kidneys: Both kidneys show fetal lobulation quite distinctly. The right kidney has a capsule which strips readily and leaves a smooth and glistening surface. On section the kidney appears normal. The striations

of the cortex are rather pale in color and stand out distinctly. The glomeruli are not definitely seen. The medullary portion of the kidney shows nothing unusual. The right kidney weighs 33 gms. and measures 6 x 3.5 x 2.5 cm. The cortex is 5 mm. in thickness. The left kidney resembles the right in all respects.

Brain not removed.

Microscopical Notes. Heart. Section shows nothing strikingly unusual. There is slight hypertrophy of the muscle fibers. No evidence of acute or chronic inflammation. No increase in fibrous tissue. No vascular changes.

The lungs show what seems to be an early pneumonia. The alveolar spaces contain red blood cells, a few polymorphonuclear and desquamated epithelial cells. There is no fibrin apparent.

Spleen: There is hyperplasia of the Malpighian bodies; also considerable engorgement with red blood cells.

The mesenteric and intestinal lymph glands show also marked lymphoid hyperplasia with prominent germinating centers.

The pancreas, adrenals, kidney, uterus, thymus, tonsils, and ovaries show nothing abnormal.

Case III. L. A., colored, age four years. No. 13,713. The youngest of four children. Two others living and well. One child had been born dead. This child was born at term. Had been breast fed for seven months. Six months before his final illness the child had been sick for a day with fever and weakness. Except for this he had always been well. On March 21, 1917, the boy was sitting in a chair, and he said that his leg hurt him, and when he tried to walk it was noticed that he limped. About twelve hours later he complained of pain in the right side of his abdomen. He began to cough, lost appetite, and vomited several times. For the next four or five days he did not sleep well on account of pain in his right side. He was admitted to the hospital on March 26th. He was a rather small but well-nourished boy, mentally clear. His lungs were everywhere resonant; breath sounds vesicular. No râles were heard. The lung borders moved freely. There was a slight bulging of the whole precordium, and a rippling impulse was seen in the third and fourth interspaces. The cardiac dullness extended 1½ cm. outside of the nipple in the fifth interspace and 4 cm. to the right of the mid-sternal line in the fourth interspace. The heart sounds were very feeble. At the apex a high-pitched, blowing, slightly musical murmur was heard. This could also be made out in the axilla and over both sides of the back. There was a gallop rhythm. The second pulmonic sound was accentuated. The pulse was small and rapid. The liver could be felt two fingers' breadths below the costal margin. The urine contained a faint trace of albumin; no white blood cells, no red blood cells. Leucocytes

12,400. Wassermann 0. During his stay of six days in the hospital, the temperature varied between 98½° and 100° F. He gradually became drowsy, dyspnea became more marked, the heart sounds became more feeble, and the pulse more rapid. He died in coma on April 2d.

Autopsy by Dr. Clark. The body is that of a well-nourished black male infant, 97 cm. in length. There is no edema to be made out in the extremities or the dependent parts. The costochondral junctions are not enlarged, nor do the epiphyses of the long bones show anything unusual. The thorax and abdomen are symmetrical. On removing the sternum the lungs do not collapse to any extent. The pleural membranes of both sides are quite smooth, delicate, and glistening, they show no fibrous or fibrinous adhesions, and neither pleural space contains any excess of fluid. There is a small *thymus* in the upper anterior mediastinum which weighs *8 gms.*

The heart occupies its usual position, but is greatly enlarged. Fig. 3 is a reproduction of a post-mortem photograph. The epicardial membranes are smooth and glistening, though there is present some fibrin in the pericardial fluid. The subepicardial fat is not increased. The heart extends about half the distance between the mid-line and the right chest wall and extends practically over to the left chest wall, displacing the left lung upward. This enlargement, however, appears to be due to a considerable degree to dilatation of the various chambers of the heart, especially of the auricles. On opening the heart the chambers are lined throughout everywhere by a smooth, delicate endocardium. The right auricle is quite markedly dilated and is filled by a large clot, which appears to be entirely post-mortem in character and presents no evidence of ante-mortem thrombus formation. The leaflets of the tricuspid valve are exceedingly delicate, as are also the chordæ tendinæ and papillary muscles. No marginal vegetations or thickenings are to be seen. The chamber of the right ventricle has a thin wall. This thinness is accounted for by the extensive dilatation. The leaflets of the pulmonary artery show nothing unusual. They are thin, semi-translucent, and delicate. The chamber of the left auricle, like that of the right, is filled by a large, red and yellowish clot, but presents no evidence of ante-mortem thrombosis. The leaflets of the mitral valve do not present anything abnormal in appearance. The leaflets of the aortic valve are also like the other valves, delicate, and present nothing of interest. The aorta is quite yellow, smooth, elastic, and shows nothing unusual. Dissection of the coronary arteries shows nothing unusual. The heart weighs *160 gms.* (The average at this age is: Bovaird and Nicoll (1) 72 gms.; Virordt (2) 74.7 gms.) The measurements are as follows:

Tricuspid ring	8.0 cm.
Pulmonary ring	4.5 cm.
Mitral ring	8.0 cm.
Aortic ring	4.5 cm.
Right ventricular wall	1.0 mm.
Left ventricular wall	10.0 mm.

Lungs. There is a slight edema of these organs. The pleural surfaces are entirely smooth and glistening, and the lung substance, as seen through the pleural surface, has the usual pinkish, mottled appearance. On palpation the lungs are more voluminous than usual and have a boggy consistency. This bogginess appears to be due to an increase in fluid within the lung substance and is quite uniform in distribution. There do not appear to be localized areas of consolidation or unusual softening. From the cut surface, which has a slightly mottled appearance, there exudes a large amount of frothy fluid. The various cut surfaces at different points are quite uniform in appearance and present quite a similar picture. The dissection of the bronchi shows them to be filled with a large amount of frothy fluid. Dissection of the vessels shows nothing unusual. The hilic lymph glands are small, pinkish in color, and present nothing of interest.

The spleen has about the usual appearance and consistency. The capsule is quite smooth and glistening, and through it the Malpighian bodies stand out as fine whitish dots. On section the Malpighian bodies stand out with distinctness, and the connective tissue architecture is not increased. The vessels show nothing unusual. The spleen weighs 41 gms. and measures 7 x 5 x 2.5 cm.

The pancreas appears normal. It is 12 cm. in length and weighs 40 gms.

The stomach and intestines appear normal.

The liver is somewhat increased in size. It extends to the umbilicus below and displaces the diaphragm slightly upward. The capsule is smooth and the cross-section appears normal. The vessels and bile ducts do not show anything unusual. The liver weighs 680 gms. and measures 19 x 10 x 5 cm.

The kidneys seem normal. Each kidney weighs 90 gms. and measures 9 x 4 x 3 cm. The left kidney resembles the right in all respects.

The adrenals occupy their usual positions at the upper poles of the kidneys and externally and on section show nothing unusual. The adrenals together weigh 8 gms.

Microscopical Notes. Heart: Section of the heart shows what appears to be a normal picture. There is no increase in connective tissue. The vessel walls have their usual thickness, and there are no areas of chronic

or acute inflammation. The muscle cells do not appear to be unusually large.

Lungs: Certain areas show alveoli which contain a pink granular material. Otherwise the lung shows nothing unusual. There is no evidence of chronic passive congestion or acute inflammation.

The liver shows a slight fatty change which is uniformly distributed throughout the lobules. There is no evidence of chronic passive congestion.

The pancreas, kidneys, adrenal, spleen, tonsil, thymus, and mesenteric lymph glands show nothing unusual.

Case IV. E. S., colored, age ten months, No. 14,536. The youngest of seven children. Under observation from birth. Birth weight 3390 gms. Breast fed. She had had a few attacks of rhino-pharyngitis and when three months old developed mild pertussis. Had been well for three or four months before her admission to the hospital. At nine months she had an attack of rapid respiration without fever and thereafter seemed well. A month later, on April 18th, she had what her mother described as a "fainting spell" and a "cold sweat." She became very apathetic and somnolent; no distinct febrile reaction. There was loss of appetite. For a few days she had been coughing with some respiratory distress. She was brought to the hospital on April 22d, a well-nourished child with slight evidences of rickets, presenting the picture of extreme dyspnea with cyanosis; respirations very rapid. She was very restless. The lungs were clear. The heart was distinctly enlarged, both to right and left, extending beyond the nipple on the left side, though its exact extent was difficult to determine. Heart sounds feeble. There was gallop rhythm; no murmurs. Fig. 4 is a copy of an *x*-ray made at this time. The spleen could not be felt. There was no edema. At the time of admission her white cells were 15,000 and temperature normal. A few hours before death the temperature rose to 102½° F. and she died twenty-four hours after admission.

Autopsy by Dr. Bullard. The body is that of a well-developed colored female of ten months, weighing 7 kilo. and measuring 67 cm. in length.

The *thymus* is enlarged and occupies the usual position in the upper anterior mediastinum. It appears edematous on section. *Weight 22 gms.*

Heart: This occupies the usual position, but is greatly enlarged, as shown by Fig. 5, a copy of a post-mortem photograph. The pericardium is smooth and delicate externally and internally; pericardial sac contains no excess of fluid. The chambers of the heart are all lined with smooth, delicate endocardium. The valves are well formed, smooth, and delicate. There are no ante-mortem thrombi. Tangential section of the musculature shows the usual homogeneous red-brown surface. The coronary vessels appear normal. The aorta, pulmonary artery, and large veins are normal in size

Fig. 1. Roentgenogram of Chest of S. C., Taken Two Months before Death

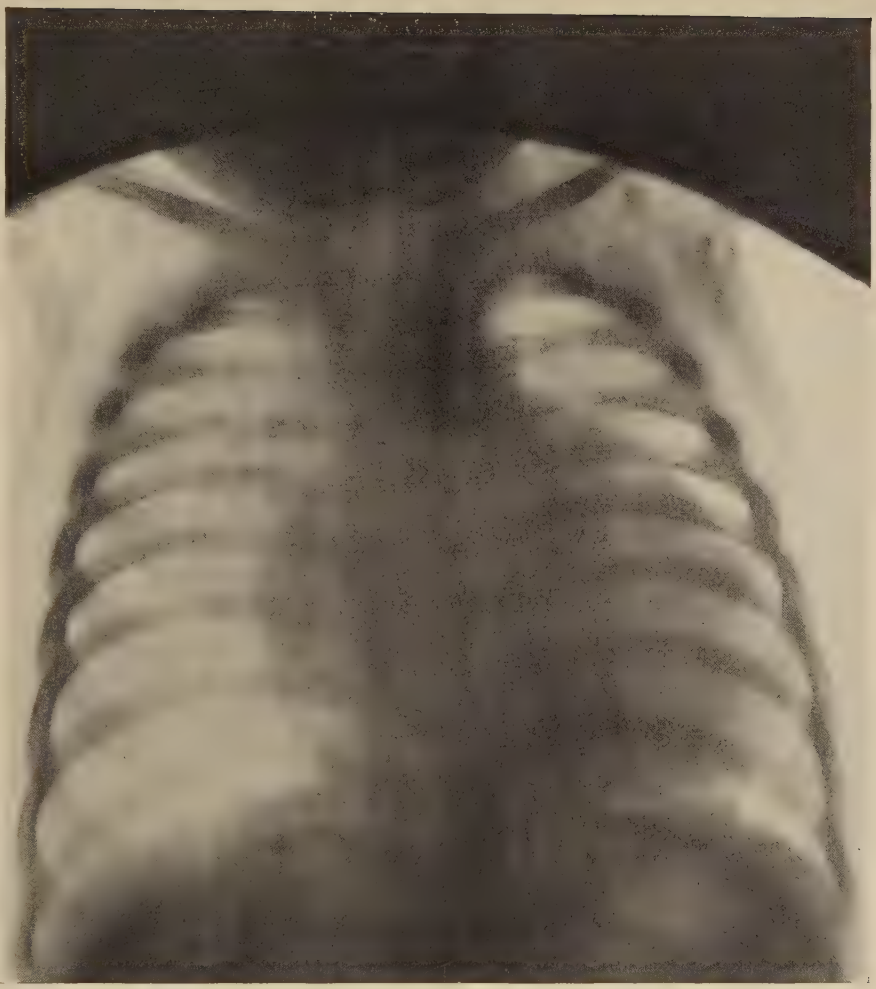

Fig. 2. Roentgenogram of Chest of G. S., Taken a Few Days before Death. Another *x*-ray Taken a Month before had Shown the Same Cardiac Enlargement.

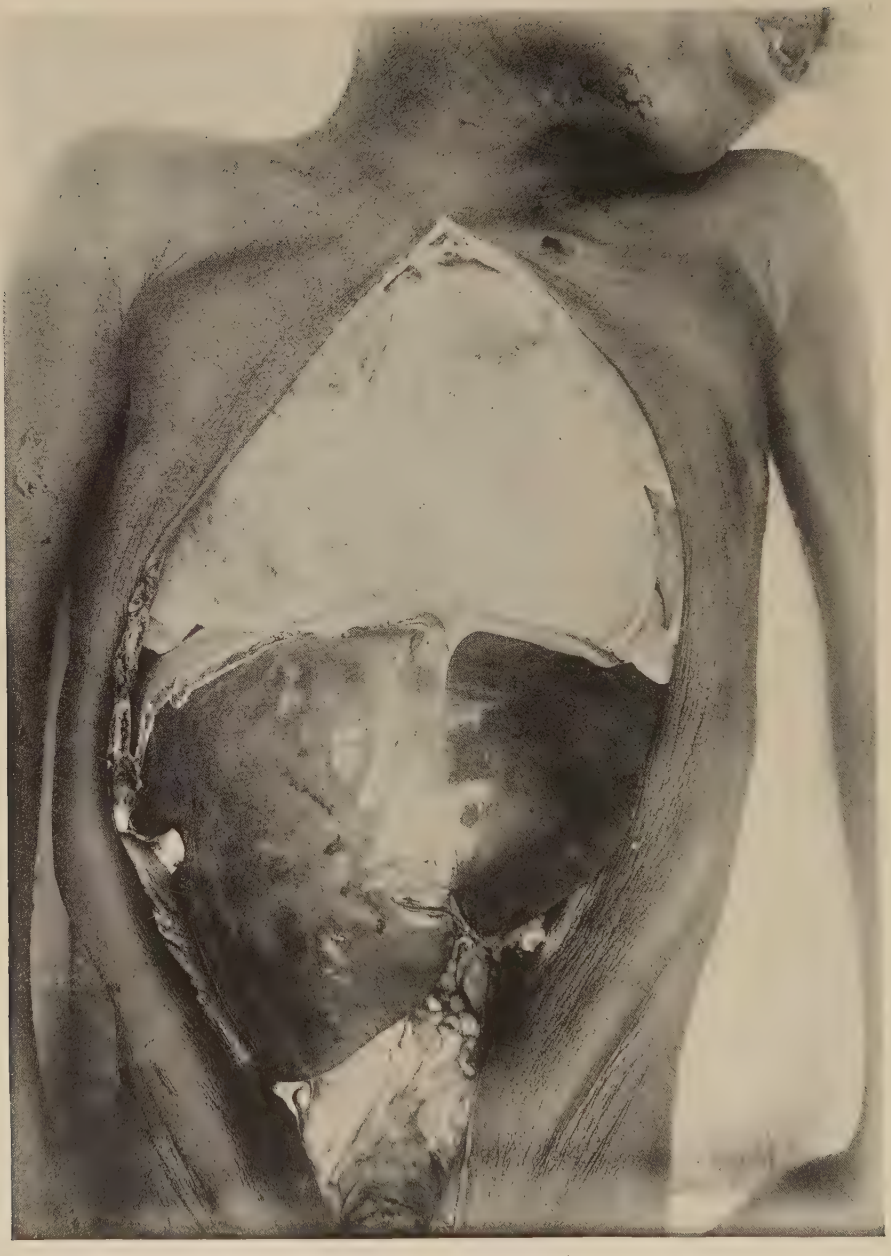

FIG. 3. PHOTOGRAPH OF L. A., TAKEN POST-MORTEM.

Shows Part, but not All of the Cardiac Enlargement. Much of the Heart on the Right Side was Covered by Lung.

Fig. 4. Roentgenogram of Chest of E. S., a Few Hours before Death.

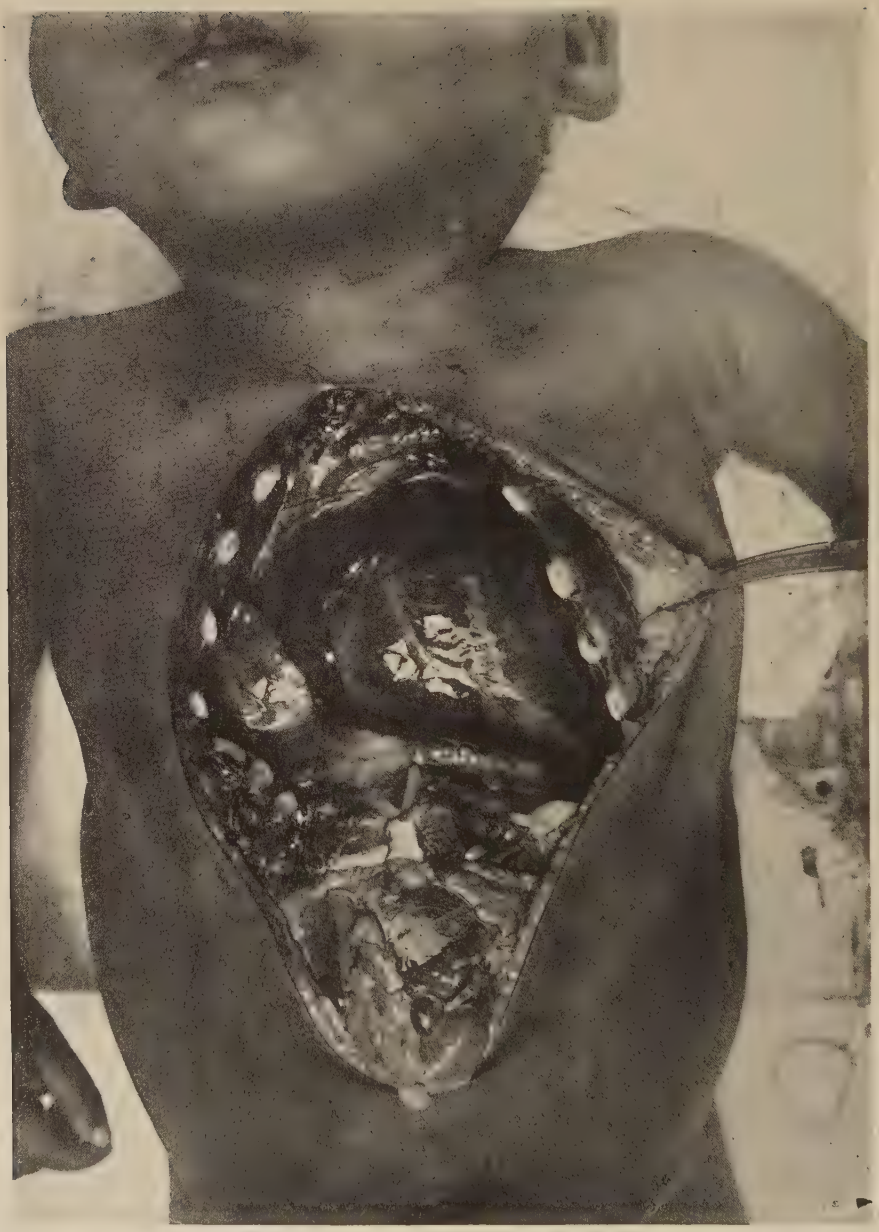

FIG. 5. PHOTOGRAPH OF E. S., POST-MORTEM, SHOWING GREATLY ENLARGED HEART.

FIG. 6. ROENTGENOGRAM OF CHEST OF O. D., THREE DAYS BEFORE DEATH.

FIG. 7. PHOTOGRAPH OF O. D. POST-MORTEM.
Great Enlargement of the Heart Readily Apparent.

and general relations. There is a cord-like remnant of the ductus arteriosus. The foramen ovale admits the tip of a probe. The heart weighs *100 gms.* (The average weight for this age is: Bovaird and Nicoll (1) 34 gms.; Vierordt (2) 33.3 gms.) The measurements are:

Tricuspid ring	6 cm.
Pulmonary ring	3.5 cm.
Mitral ring	5.5 cm.
Aortic ring	3.3 cm.
Base of aorta	3.0 cm.
Right ventricular wall	2.0 mm.
Left ventricular wall	8.0 mm.

Lungs collapse normally on exposure to atmospheric pressure. Pleural surfaces are smooth and delicate; no excess of fluid in the pleural spaces. Both lungs are air-containing and crepitant throughout; no areas of consolidation are made out. The bronchi and vessels appear normal. Bronchial lymph glands have the usual size, shape, and consistency.

Spleen externally appears normal. On section the splenic nodules are made out. Splenic pulp is dark red and of the usual consistency. No increase in connective tissue. Spleen weighs 20 gms. and measures 6 x 3.5 x 1.5 cm.

Liver occupies the normal position and is large. The usual liver architecture is made out through the smooth, delicate capsule and on section. The liver weighs 350 gms. and measures 15 x 9 x 4.5 cm. The gall-bladder is smooth, delicate, and undistended; it contains thick amber bile, which flows freely from the ampulla of Vater.

Kidneys occupy the normal position and have the usual size, shape, and general appearance. The capsule is delicate and strips easily, leaving a smooth, red-brown surface on which the stellate veins are seen. On section the architecture of cortex and medulla is made out as usual. The vessels are normal.

Pancreas is normal to gross examination.

Stomach and duodenum: The stomach contains white curds. The duodenum contains bile-stained fecal matter. The mucosa of both shows only post-mortem changes. The musculature shows nothing noteworthy.

Intestines: The serosa is smooth and delicate throughout. The peritoneum contains no excess of fluid. The musculature of the intestine is normal. The mucosa is pale and delicate throughout. No hypertrophy of the lymphoid tissue. The mesenteric and retroperitoneal glands are normal in size, shape, and consistency.

Microscopical examination of the viscera shows them to be essentially normal.

Case V. O. D., colored, two years, No. 18,737. Father, fifty-eight, mother, thirty-two, living and well. The seventh of eight children, all living and well except the patient. His weight at birth was not known, but he was a well-developed child. His health in infancy had been good. He was breast fed for nearly a year and a half. He began talking at a year; had never walked. Had never suffered from any illness except an occasional cold or cough until the present illness. About three or four weeks before admission to the hospital, his legs began to swell. After a few days the swelling subsided, but returned again before his admission to the hospital. There had been no evidence of pain, but he had seemed short of breath for four weeks, though there had been no orthopnea. He had been somewhat somnolent and less active than usual. His appetite had been good, there had been no vomiting, and his bowels had moved once or twice each day. He had had no fever. He was admitted to the hospital on August 5th. His temperature was normal; respirations 32; pulse 112; weight 20 pounds. There were no abnormal signs in his lungs. Respirations slightly accelerated and somewhat labored. The heart's apex was in the sixth interspace and the heart was greatly increased to right and left, being 3½ cm. to the right and 4 cm. to the left of the median line. No definite murmur made out. Sounds rather indistinct. Fig. 6 is a copy of an *x*-ray made on his admission to the hospital. Pulse accelerated, but of fair quality. Blood pressure 88/68. Liver was readily felt two fingers' breadths below the costal margin. It was not tender. His spleen was palpable just at the costal margin. There was a slight enlargement of the epiphyses, but his chest was not rachitic. His white cells were 7760. Urine cloudy, dark in color; specific gravity 1025; marked amount of albumin present and microscopically a few white blood cells and an occasional red blood cell but no casts. His 'phthalein output was more than 53 per cent in two hours. His Wassermann reaction was negative and two Pirquet reactions were negative. The child's condition did not improve. Temperature rose to 104° F. three days after admission, but fell rapidly, and for the last twelve days in hospital was normal. The edema increased somewhat. The abdomen became tense and distended, his respiratory distress became greater, the pulse became very rapid and feeble, he ceased taking nourishment, and for the last forty-eight hours was in stupor most of the time. On August 22d he died suddenly, his condition having apparently been no worse than for several hours before.

Autopsy by Dr. Bullard. The body is that of a well-nourished, colored, male infant, 72 cm. in length. Body weight 8.2 kilo. The subcutaneous tissue shows a most marked edema. The thymus gland is not enlarged. The right pleural sac contains about 80 c.c. of clear, yellowish fluid. The left

sac, about 40 c.c. of a similar fluid. There are no pleural adhesions and the surfaces are everywhere smooth and of a normal luster.

Heart: The pericardium contains about the normal quantity of clear fluid. Both layers of the pericardium are everywhere smooth and of normal luster. The heart is enormously enlarged. (Fig. 7 is a copy of a post-mortem photograph.) It extends to the ribs in the left anterior axillary line. To the right the heart extends somewhat lateral to the mammillary line. It weighs *110 gms.* (Average weight at this age: Bovaird and Nicoll (1) 58 gms.; Vierordt (2) 51.9 gms.) The epicardium is everywhere smooth and of normal luster. The apex of the heart is distinctly bifid. The left auricle is not enlarged to the same extent as are the right auricle and ventricle. The left auricular appendix is only slightly larger than normal, while the right auricular appendix is three or four times as large as the left. The auriculoventricular groove is unusually prominent. On opening the heart the endocardium is everywhere smooth. In the left ventricle, however, particularly over the ventricular septum, the endocardium is abnormally opaque. The large vessels which enter and feed the heart show no abnormalities in distribution or general arrangement. The foramen ovale and ductus Botalli are closed. The cavities of the right auricle and ventricle and of the left ventricle are all very much larger than normal. This is most marked on the right. The left ventricular wall is only slightly thicker than normal, but because of the notable dilatation of this chamber of the heart, the amount of the muscle tissue is much greater than that to be found in a normal heart. The valves of the heart show nothing abnormal. The cordæ tendinæ are not thickened. In order to preserve the specimen, the heart is not opened up in the usual manner. The measurements of the heart valves are therefore not recorded.

Lungs: The right lung is voluminous, elastic, and air containing. The pleural surface is everywhere smooth and of normal luster. On section much frothy fluid covers the cut surface. The tissue is everywhere elastic and air containing. The lymph glands at the hilum of the lungs are not enlarged. The blood vessels and bronchi likewise show nothing abnormal. The left lung resembles the right.

Spleen weighs 19 gms. The capsule is smooth. The pulp is red and firm, of a dark-red color. The Malpighian bodies stand out with moderate distinctness, and of about the usual size. The trabeculæ are not thickened.

The pancreas seems rather large. It weighs 18 gms. The lobules are distinctly outlined. The tissue shows nothing abnormal.

Stomach and duodenum are not abnormal.

The liver is rather large. It weighs 260 gms. The capsule is everywhere smooth, thin, and transparent. The liver tissue is of moderate consistency

and contains much fluid blood. On the surface and on section the lobules stand out distinctly. The gall bladder contains 6 c.c. of thick, brownish-yellow bile. The cystic and common bile ducts are patent.

The kidneys together weigh 70 gms. The capsule of the right kidney strips easily, leaving a smooth, grayish-red surface. On section the kidney tissue contains much fluid blood. The striæ of both pyramids and cortex are distinctly marked and show no distortion. The kidney pelvis shows nothing unusual. The left kidney resembles the right in size and general appearance.

The pelvic organs, neck organs, and aorta show nothing unusual.

Stomach and intestines: The mucosa of the small intestine and colon is much congested throughout. In other respects they show nothing unusual. Peyer's patches and the solitary lymph follicles are not enlarged.

Cases similar to the above have been reported very infrequently. In all, including these 5, I have not been able to find more than 20 that could be classed in this category, and of these 20 some are open to criticism. But I believe with Oberndorfer (3) that the condition cannot be so extremely rare, otherwise it would have been impossible for him to see 5 cases in a single year, and I should not have seen 5 cases in two years, in a not very large hospital service. I also can remember to have seen similar cases years ago in New York when doing autopsies in large number at the New York Foundling Hospital. In the absence of an explanation for the hypertrophy, the condition failed to attract the attention that it should have.

Bednar (4) as early as 1852 stated that cases of cardiac hypertrophy that he had seen affected children in the first two months of life. This hypertrophy was accompanied by dilatation of the aorta or stenosis of the aorta or pulmonary artery, and often there was hypertrophy of the thymus or thyroid and sometimes of the liver and spleen. It is quite impossible to make out from his descriptions whether he had seen a case of pure cardiac hypertrophy or whether the hypertrophy was always complicated by some other condition.

Mayr (5) was one of the first to mention unexplained enlargement of the heart, but he did it merely in the statement that "a congenital hypertrophy of the entire heart was to be found in the newly born combined with an enlargement of the liver, spleen, thyroid, and thymus; without cyanosis, ending usually with hyperæmia or inflammation of the lungs."

It is also quite impossible to make out what it was that caused the enlargement that Beneke (6) or Henoch (7) (8) described. The latter asserted that he had seen hypertrophy of the heart "in two small children who probably from birth had large hearts." The descriptions of cases by Hauser (9), Heubner (10), and others are also not sufficiently clear. They are too abbreviated or the weights of organs are not given or other pathological processes were present that might have produced hypertrophy. Certainly the first clear and readily available description of a case, if not the first case described, is that by Simmonds (11). It is likely, however, that Vollbeding (12) saw a characteristic case, but his article is difficult of access on account of its appearance as an inaugural thesis. In the last few years Efron (13), Hedinger (14), Kaufmann (15), Kalb (16), Mischaud (17), Oberndorfer (3), and Ratner (18) have placed cases on record.

Objection has been raised to the inclusion of some of these cases, such as those of Kalb (16), Hedinger (19), and Ratner (18), among those of idiopathic cardiac hypertrophy, because there was at the same time a considerable enlargement of the thymus gland or the evidences of status lymphaticus. Thus in Kalb's (16) case the thymus was "as large as a hen's egg," in Hedinger's (19), that he refused to include for this reason, the thymus weighed 23.7 gms., in one of Oberndorfer's (3) the weight was 22 gms., and in one of the series here reported the weight was 22 gms.

It is difficult to see why a moderate enlargement of the thymus should invalidate all such cases. For in reality we do not know accurately the limits of size or weight of the normal thymus. There seems little doubt that it varies much, if one may judge from the results of post-mortem examinations upon infants and young children dying quickly, as the result of accident or disease. If the enlarged thymus were associated with enlargement of the thyroid or other organs such as the liver and spleen, and if the finding were observed in a dead-born fetus or in an infant surviving only a short time, there would seem to be every reason for eliminating such a case from the category of idiopathic cardiac hypertrophy. It does not seem to me necessary to do so when the weight of the thymus is not greater than 20 to 25 gms. A thymus of this size is not infrequently found when the cause of death clinically and by post-

mortem examination has been perfectly plain and no symptom whatever has been present to indicate that any abnormality of the thymus was present. Moreover, how does an enlargement of the thymus cause hypertrophy of the heart? It is very easy to say that it might, theoretically, by pressure on the great vessels, thus producing an obstruction to the flow of blood in the aorta or pulmonary artery. But much greater enlargement of the thymus is frequently found with no cardiac enlargement, and even in the most extreme cases of status lymphaticus, hypertrophy of the heart is not a part of the pathological picture. The tabulated figures in the article by Bovaird and Nicoll (1) upon weights of the viscera in infancy show no relationship to exist between the weight of the thymus and that of the heart. Occasionally with enlargement of the thymus the weight of the heart is increased, but the increase is moderate.

The right to inclusion of other cases such as that reported by Hauser (9) has been questioned on the ground that prolonged pertussis or pulmonary disease would cause cardiac hypertrophy. The observers refer to the statement of Dusch (2) that cardiac hypertrophy may be caused by prolonged disease of the lungs, such as atelectasis or pneumonia. Pulmonary conditions do cause an increase in the weight of the heart, as the figures of Bovaird and Nicoll (1) well show, but it is not an increase amounting to several hundred per cent. That such a change may result from pertussis is seriously to be questioned.

What may cause great enlargement in early infancy? There are two conditions with which it is chiefly found: (1) congenital malformation of the heart or great vessels and (2) marked rickets of the thorax. It is not necessary to discuss the method of the production of the hypertrophy in these circumstances, for in the cases under discussion there was no discoverable lesion of the valves, the septa, the vessels, or the cavities other than dilatation, and no distortion of the chest. Factors that are held responsible in older childhood, such as excessive exercise, overeating and drinking, nephritis, etc., may be dismissed from consideration. They are not operative in early infancy.

The causes that have been suggested to account for this cardiac hypertrophy have been hypothetical and for that reason quite unsatisfactory. Virchow (21) suggested that there might be a dif-

fuse rhabdomyoma of the heart. The uniformity of the hypertrophy in many of the cases would make this most unlikely. A chemical stimulus in the blood has been suggested. Hedinger (14), impressed by Wiesel's work, supposed excessive stimulation from the side of the chromaffine system, and urged biological study of this system. Mischaud (17), apparently to guard against the eventuality of hypoplasia of the chromaffine system being found, rushed to the rescue with the suggestion that the lack of sufficient secretion might produce a dilatation of the heart which would hypertrophy secondarily to compensate for the dilatation.

The use of these hypotheses, quite impossible of substantiation, serves to indicate the obscurity of the condition, as does also the suggestion that it results from "some disturbance of intrauterine circulation." This last suggestion emphasizes the fact that an explanation must be found for what is very generally considered to be a congenital condition. Whether it always is, it is quite impossible at present to say. That it frequently is, is shown by the fact that two of the cases reported were in infants born dead (Simmonds (11), Oberndorfer (3)) and another in a three-months-old infant. Except for these, the children have been six months of age or more up to four years. It is difficult to conceive of any condition in extrauterine life that would bring about such a rapid and great hypertrophy, but it is equally difficult to conceive of an intrauterine condition that would do the same. One could only speak with assurance regarding extrauterine hypertrophy if one could exclude definitely hypertrophy in an infant who subsequently was found to have it. This up to the present time has been impossible. The only patient that has been observed for a long time was G. S. of our series. She certainly gave no evidence of cardiac disturbance during the many months that she was under observation. When we saw her again after an interval of three months there was no doubt that she was in distress, and the physical examination at this time, as well as the *x*-ray, pointed to a cardiac hypertrophy, which was not less marked than it was at the time of her death a month later.

A few patients have not manifested any symptoms until they were many months of age (2½ years, three years, four years, 4½ years), which would make it seem possible if not probable that the hypertrophy has been late in developing. It is a striking fact that

with hypertrophy alone, without any myocardial degeneration or infiltration, an hypertrophy affecting sometimes one ventricle more than the other and sometimes the whole heart uniformly, the break in compensation should be so disastrous. In almost all the recorded cases up to the present time the final catastrophe has been of short duration, a matter usually of a few hours or days. Less frequently there have been the premonitory symptoms of fainting attacks or temporary dyspnea, but when the symptoms have been well established the progress has been rapid from bad to worse.

There has been some discussion regarding the enlargement of these hearts, as to whether it was all to be explained on the basis of an hypertrophy of the fibers. So far as our cases give testimony it is to the effect that hyperplasia must play a part. While in one or two instances there was a distinct increase in the size of the fibers, in others there was no notable change from the normal. There would seem to be nothing impossible in the assumption, especially if the condition is congenital, that there actually is an increase in the number of fibers.

Hedinger has stated that it is practically impossible to make a diagnosis of this condition. This has not been our experience. We have correctly appreciated the condition four times. It is quite true that if an infant is observed only in the last few hours or minutes of life, a satisfactory diagnosis is out of the question, for then fever is often present, and the great dyspnea renders an accurate examination of the heart and lungs impossible.

If there are some hours or days for observation, a diagnosis should be made, in certain instances at least. The history of attacks and the presence of dyspnea in the absence of evidence of pulmonary or congenital cardiac disease are enough to arouse suspicion. There are generally no murmurs. If they are heard, they are usually blowing murmurs in contrast to the rough, harsh murmurs of congenital cardiac disease. Edema is not a common symptom with this form of cardiac hypertrophy, but if it is present it serves to focus the attention upon the heart provided severe nutritional disturbance, congenital cardiac disease, nephritis, and other causes of edema may be excluded. Cyanosis is usually absent or not marked, in contrast to the graver forms of congenital cardiac disease, which are accompanied by cyanosis more often than by edema. It is difficult to

make out accurately the outlines of the heart, but with such an hypertrophy as is present in these cases the enlargement should not escape detection. Finally corroborative evidence is furnished by the *x*-ray. The increase in the cardiac shadow is striking.

At the present time it is impossible to say if there are slighter grades of hypertrophy that may be recovered from or compensated for. They have not as yet been recognized. We know only the clinical picture of the terminal stages and that in the terminal stages any attempt at treatment is without avail.

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WHAT THE WAR HAS TAUGHT US ABOUT HYSTERIA

By Arthur F. Hurst, M.A., M.D. (Oxon), F.R.C.P.

Temporary Lieut.-Colonel, R.A.M.C., Officer in charge of Seale Hayne Military Hospital, and Physician and Neurologist to Guy's Hospital

SINCE August, 1916, my time has been devoted to the study and treatment of soldiers suffering from war neuroses. This has afforded me an almost unique opportunity of investigating hysteria in men, particularly during the last year, when I have had a band of ten enthusiastic workers[1] studying these problems with me at the Seale Hayne Military Hospital.

Gradually our views have altered, and while we are still convinced that the traditional conception of hysteria, which has been handed down by the innumerable physicians who studied under Charcot, is incorrect, we are no longer blind followers of Babinski, and have, we believe, learnt lessons from our experience of war hysteria which will fundamentally modify our attitude towards many of the medical problems of civil life.

Perhaps it will be simplest to begin with a definition of hysteria, which we have found fits in with the facts better than any other with which we are familiar. It is similar to Babinski's definition, but differs from it in certain important particulars.

Hysteria is a condition in which symptoms are present which have been produced by suggestion and are curable by psychotherapy. The forms of psychotherapy we chiefly use are explanation, persuasion, and re-education, which are generally preferable to gross methods of suggestion, whether in the waking state or under hypnosis, as the patient is taught to take an active part in his own cure and is consequently less liable to relapse.

According to this definition hysteria does not exist apart from hysterical symptoms. Charcot, on the other hand, taught that hysteria manifests itself in two ways—by obvious symptoms, which

[1] J. L. M. Symns, S. H. Wilkinson, W. H. Raynell, J. W. Moore, A. W. Gill, G. McGregor, C. H. Ripman, R. G. Gordon, J. F. Venables, A. Robin.

are more or less temporary, and stigmata, which are present before the obvious symptoms appear and persist after their disappearance. We believe that this is wrong, and that the patient is not suffering from any definite malady except when hysterical symptoms are present.

The so-called hysterical stigmata were supposed to be of two kinds, mental and physical. There is such diversity of opinion as to the character of the mental stigmata that considerable doubt must at once be felt about their constancy and importance, as, if they were invariably present, it should be easy to obtain agreement on the subject. Perhaps the most common view of the mental state present in hysteria corresponds with the lay idea of an hysterical person, typified by an emotional, excitable girl, who easily goes into "hysterics." It is true that a girl of this kind is liable to develop hysterical symptoms, but she has nothing in common with many of the unemotional, stolid soldiers who have developed hysterical symptoms during the war.

Babinski's teaching would lead to the idea that the hysterical individual is one who is abnormally suggestible. This would include the typical hysterical girl, as well as those soldiers who as a result of the stress and strain of active service have become abnormally suggestible, and develop hysterical symptoms with slight provocation. But it does not include all cases of hysteria, as I am convinced that there is no man who would not develop hysterical symptoms if the provocation were sufficiently great. Unless everybody is suffering from hysteria, it follows that there is no constant mental state which is present both before the active symptoms develop and after their disappearance. Abnormal suggestibility bears the same relationship to hysteria that a tuberculous family history does to phthisis. Just as a girl whose parents have died from tuberculosis is abnormally liable to develop tuberculosis herself, although she cannot be called tuberculous unless tubercle bacilli have invaded the tissues of her body, so the typical "hysterical girl" cannot be considered to be suffering from hysteria unless she develops obvious hysterical symptoms, which she may never do in spite of her abnormal suggestibility.

Practical results of greatest importance follow the acceptance of the view that there is no constant hysterical mental condition

and that hysteria may occur in anybody, however greatly he may differ from the traditional conception of an hysterical individual. It will be found that hysteria is more common than has been supposed, and that many conditions regarded as organic are really in part or wholly hysterical. The success of the bonesetter and the Christian Scientist with patients, whom physicians and surgeons have failed to cure, depends almost entirely upon suggestion, and is due to the fact that the latter have not recognised the hysterical nature of the malady owing to the absence of the supposed hysterical mental stigmata.

The investigations of Babinski have demonstrated the fallacy of the physical stigmata of hysteria. He has shown that the anæsthesia, which is supposed to be so characteristic of hysteria, is the result of unconscious suggestion on the part of the observer. Like him we have failed to find it when great care has been taken to avoid suggestion, unless the patient has already been examined, and we have confirmed his views by a number of new observations. We have, for example, found that the typical anæsthesia of hysteria is nothing more than the anæsthesia which an average individual with no knowledge of anatomy or physiology would expect to be present (1). Thus we asked 27 healthy young men to pretend that they were attempting to swindle a railway company after an accident by malingering paralysis of the right arm and leg. We then told them to describe in detail any other symptoms which they had besides the hemiplegia. None mentioned anæsthesia. They were now asked whether they felt as well on the hemiplegic side as the other: 23 replied in the negative, this corresponding to the first stage in the suggestion of hysterical anæsthesia. On going into details as to the extent of their anæsthesia 11 described it as hemianæsthesia and 12 as anæsthesia of the whole arm and whole leg. Glove and stocking areas were described when they were asked what they would expect the extent would be if the paralysis were confined to the hand and foot. The areas of anæsthesia thus correspond exactly with those regarded as typical of hysteria. To show how easily true anæsthesia can be suggested by the ordinary methods of examination, Symns, Gainsborough, and I asked 28 men, who were deafer in one ear than the other owing to organic disease, which side they felt better when both ears were lightly touched (2). It was

found that this simple examination resulted in anæsthesia of the deaf ear in 18 cases, which was so marked in one man that he was afterwards seen putting pins through the lobe for the amusement of his fellow patients, although none had any hysterical symptoms or was in any way neurotic.

Babinski has shown that the constricted field of vision, which was one of Charcot's hysterical stigmata, does not exist if a method is used which is less liable to suggest abnormalities than the perimeter. Symns and I (3) confirmed his observations, and found, moreover, that the inward spiral field of vision, which is generally regarded as pathognomonic of hysteria, is simply due to the usual method of examining with a perimeter, as when the disc is moved outwards instead of inwards, outward spirals are obtained, and in several cases we obtained an inward spiral with one eye and an outward spiral with the other, or an inward and outward one successively in the same eye, according to the direction the disc was moved.

Just as the so-called physical stigmata of hysteria may be unconsciously suggested by the observer in patients suffering from organic disease as well as from hysterical symptoms, so may certain physical signs, which are supposed to help in the diagnosis of organic visceral disease, be unconsciously suggested, and must thus sometimes be of the same character as the "hysterical stigmata." Thus I am convinced from observations extending over eleven years that Head's areas of cutaneous hyperæsthesia are very rarely present until they have been unconsciously suggested by the observer, their frequency being in inverse ratio with the care taken in avoiding suggestion. My first doubt on the subject arose when I had been unable to find any trace of hyperæsthesia in six consecutive cases of duodenal ulcer, in which the diagnosis was confirmed by operation, although I had hitherto found definite areas in the majority of patients whom I regarded at that time as suffering from gastric ulcer, though no operation or post-mortem confirmation was available. I soon came to realise that the majority of patients in whom Head's areas were found were abnormally suggestible. Thus the gastric area is constantly found in chlorotic girls who suffer from epigastric pain and hysterical vomiting and who were formerly believed to be suffering from gastric ulcer, although this is now known to be rare in such individuals, though comparatively com-

mon at a later age, especially in men, and in these cases cutaneous hyperæsthesia is rarely found owing to their much slighter degree of suggestibility. The areas of deep referred tenderness described by Mackenzie are equally likely to be produced by suggestion. Certain observers have found tenderness of the intercostal muscles over the præcordium in a large proportion of men suffering from "soldier's heart," but in fifty cases in which care was taken to avoid suggestion I did not find it once. In the same way McBurney's point is constantly found to be tender in appendicitis by those who believe in it, but rarely by those who do not, and my radiographic observations have confirmed the investigations of others that the local tenderness in chronic appendicitis is always over the inflamed appendix, and is over McBurney's point only when the appendix happens to be there; if the cæcum and appendix are displaced by manipulation with one hand, the tender point is correspondingly displaced.

The next part of the definition of hysteria to consider is the statement that the symptoms are produced by suggestion and curable by psychotherapy. This at once excludes all those cases which have been ascribed to hysteria whenever no other explanation could be found for the condition which was present. With improved methods of investigation their number has steadily diminished. A definition which would have correctly led in a given case to a diagnosis of hysteria ten years ago but of organic disease to-day is obviously absurd. There are no such things as hysterical fever, hæmorrhage, and œdema, as they can neither be produced by suggestion nor cured by psychotherapy, although they are still described in most modern text books.

I believe that the most common source of suggestion of hysterical symptoms is some organic disease or injury, the symptoms resulting from which are perpetuated or aggravated by auto-suggestion, sometimes with the help of the unconscious hetero-suggestion, produced by the questions and the treatment recommended by the physician if he does not recognise the true nature of the condition. When thus produced, hysterical symptoms always simulate the organic symptoms which preceded them more or less closely. In many cases when a certain degree of improvement has occurred in the original organic condition, a mixture of an organic basis with a

superimposed hysterical element is present. I believe that this is a much more common event than is generally supposed, and that every organic incapacity tends to suggest a greater incapacity. I believe, for example, that the spontaneous improvement, which frequently occurs in the paraplegia and amblyopia of disseminated sclerosis, is the result of some contra-suggestion, which leads to the disappearance of the hysterical paralysis or amblyopia, suggested by the slight organic paralysis or amblyopia produced by the lesion of the central nervous system. If this were universally recognised, the progress of the disease would be more uniform and less rapid, as the development of an hysterical element could be prevented, or if it had already developed it could be rapidly cured by deliberate psychotherapy. The improvement which occurs as a result of treatment by Frenkel's exercises in tabes is often largely due to the removal of an hysterical exaggeration of a slight organic ataxy, the re-education being as much a re-education of the mind, and therefore a form of psychotherapy, as re-education of the deficient muscle-sense.

A soldier was admitted with such severe ataxy that he could scarcely use his hands and could neither walk nor stand without assistance. His condition was at first regarded as hysterical, as no thorough examination of his nervous system was made. The result was that in a single sitting he greatly improved, and at the end of a week he could walk almost normally and could use his hands for all ordinary purposes. A more careful investigation then showed that he was suffering from Friedreich's ataxy, as he had all the typical signs and his brother was a complete cripple from this condition.

I believe that in every case of gradually progressive organic nervous disease, the possibility of an hysterical element should be considered. Many apparently hopeless cases would then receive the benefit of psychotherapy, which would remove any hysterical element present, although it would not influence the ultimate course of the disease. The man with Friedreich's ataxy is now capable of earning a living, but if we had heard his family history and had discovered the signs of organic disease directly after admission, we should have diagnosed the condition at once, and concluded that nothing could be done for him. I do not suggest that no history should be taken and no examination made, but a case like this shows that nothing but actually trying psychotherapy can show

whether the whole incapacity is due to the organic disease or whether an hysterical and therefore a curable element is present.

The physical signs of organic disease in such conditions as tabes and disseminated sclerosis may precede the onset of symptoms. Thus a tabetic may complain of gastric crises but no ataxy, although his knee-jerks and ankle-jerks are lost, and a patient with disseminated sclerosis may complain of nothing but loss of vision, although all the physical signs of spastic paraplegia are present. Conversely when an organic disease of the central nervous system of acute origin gradually improves, the physical signs may persist after the symptoms have completely or almost completely disappeared. If in such a case the initial incapacity suggests a perpetuation of this incapacity, then a stage is ultimately reached in which the symptoms are entirely or almost entirely hysterical, although all the physical signs of organic disease are present. In such a case the diagnosis can only be made by discovering what benefit results from psychotherapy, as the physical signs of organic disease are qualitative and not quantitative, and simply indicate that some structural change is present, without proving that any accompanying incapacity is also organic. Symns and I (4) described several soldiers with hemiplegia and paraplegia resulting both from wounds and disease, in which the symptoms at the end of even a year or two proved to be hysterical, as they disappeared rapidly with psychotherapy, in spite of the presence of physical signs of organic disease, caused by the small permanent damage done to the central nervous system by the original lesion.

The distinction between organic and hysterical nervous disorders is generally made by three varieties of signs. The first is conclusive and consists of phenomena, such as optic neuritis and atrophy and changes in the cerebro-spinal fluid, which afford visible evidence of organic disease. The second consists of those physical signs which are beyond the control of the will so completely that they can never arise from suggestion. The number of these, however, is steadily diminishing as our knowledge increases, and at the present moment the only ones which appear to be conclusive are absent knee- and ankle-jerks, extensor plantar reflex, the Argyll-Robertson pupil, a grossly irregular and eccentric fixed pupil, and the reaction of degeneration. Ankle clonus, indistinguishable from that seen in

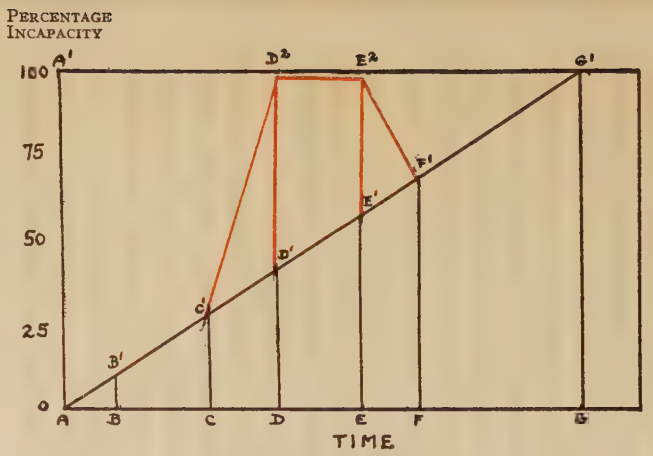

DIAGRAM I. Combined Organic and Hysterical Incapacity in Disseminated Sclerosis.

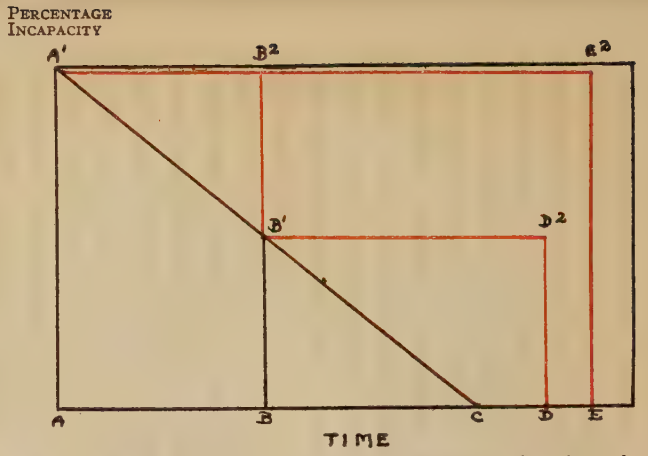

DIAGRAM II. Hysterical Paralysis Associated with Organic Paralysis, with Complete Recovery.

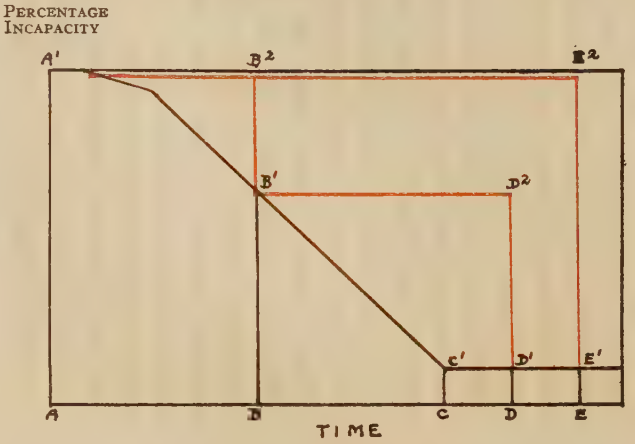

DIAGRAM III. Hysterical Paralysis Associated with Organic Paralysis, which Recovers, but Leaves Organic Physical Signs.

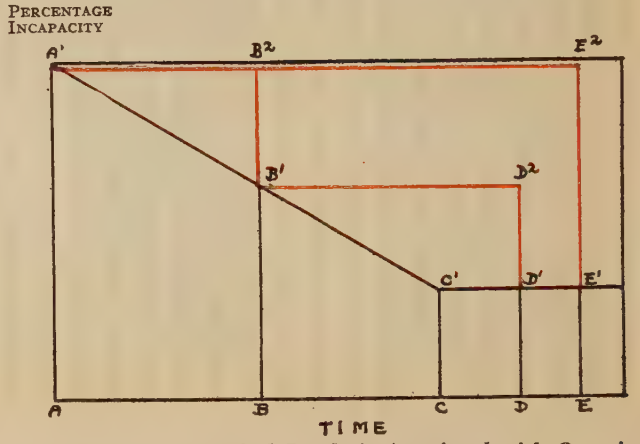

DIAGRAM IV. Hysterical Paralysis Associated with Organic Paralysis, which Recovers Incompletely.

organic disease, Babinski's "fan sign," unequal and absent abdominal reflexes, and in one case of total hysterical blindness even absolute loss of pupil reflex to light, have all been seen by us in conditions proved to be hysterical by their recovery, with the accompanying physical signs, at a single sitting as the result of psychotherapy.

The third group of physical signs consists of a large collection of symptoms which are more or less constantly present in organic disease, but which, owing to their nature, would not be likely to be simulated subconsciously in hysteria or consciously in malingering, in both of which the features of the incapacity correspond with the ordinary lay conception of the disease. Many of these signs are due to Babinski, the best known being participation of the platysma in organic but not in hysterical paralysis, pronation of the hand when tossed from a position of supination, and combined flexion of the thigh and pelvis ("Babinski's second sign"). I have looked for each of these signs in a number of normal individuals, who have been asked to pretend that they were paralysed on one side, and in almost every case they were absent, simply because an ordinary individual would not realise that they should be present. Although these signs are absent in most cases of hysterical paralysis, when the latter is the result of the perpetuation by auto-suggestion of paralysis produced by organic disease, they are no longer of any value, as the patient will have been trained by the primary organic paralysis to perpetuate it in all its details. Consequently a case of hysterical hemiplegia, which has resulted from the perpetuation by auto-suggestion of organic hemiplegia, will not only show all this third class of physical signs, but the posture assumed will be more or less identical with that of hemiplegia, so that a diagnosis cannot be made at sight, as is often possible when the paralysis is hysterical from the onset. If the primary lesion does not disappear completely, the patient will show a combination of hysterical symptoms with organic physical signs of the second class, due to the slight residual organic disease, as well as all of the third class. An accurate diagnosis by examination is then impossible, and nothing can be done except to test the effects of psychotherapy, which will have no effect on organic paralysis, but will remedy any hysterical element present.

These ideas are applicable not merely to paralysis. It is, for example, stated that hemianopia never occurs in hysteria, the most

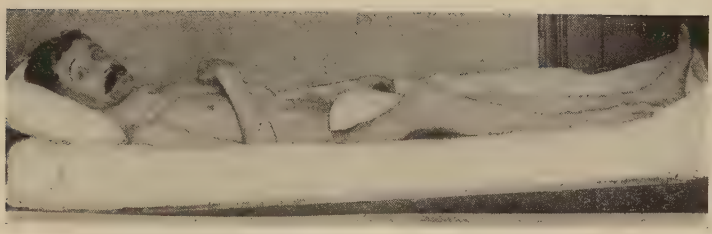

Fig. 1.

Fig. 2.

Combined Hysterical and Organic Hemiplegia of Two Years' Duration; Almost Complete Recovery with Psychotherapy.

Complete right-sided hemiplegia developed after convulsions in attack of nephritis 1.10.1916. Typical posture of organic hemiplegia with exaggerated jerks, ankle clonus and extensor plantar reflex on right side. No change when admitted in October 1918 (Fig. 1). With psychotherapy he moved arm and leg in 2½ hours (Fig. 2), and could stand after another hour; next day he walked. Typical upper neurone type of facial paralysis with platysma sign still present (Fig. 4); this was cured in 45 minutes (Fig. 5). By December 1918, he could write and do needlework, and walk almost normally (Fig. 3).

Diagram 3 on p. 607 represents a case of this sort. In each diagram the black lines indicate organic and the red lines hysterical incapacity. The original hemiplegia was all organic (AA′); later it was partly organic (BB′) and partly hysterical (B′B2), and finally all hysterical (E′E2), but with sufficient permanent damage to produce organic physical signs (EE′).

Fig. 3.

Fig. 4.

Fig. 5.

common hysterical visual defect being a general impairment of the sight. But I have seen two cases in which hemianopia was caused by a gunshot wound of the occipital lobe. The initial blindness was due in part to concussion and other evanescent changes in the surrounding tissues, so that when these had passed away the permanent lesion was insufficient to account for the hemianopia, which was due to the perpetuation of the primary organic condition by auto-suggestion. The hysterical hemianopia, which developed in this way, was rapidly cured by psychotherapy.

Epilepsy. Our experience has shown that among the large number of soldiers sent into hospital as epileptics a considerable proportion are suffering from nothing more than hysterical fits. In the absence of any personal or family history of epilepsy, and in the absence of any head injury or organic disease, such as general paralysis, almost every case has proved to be hysterical. Even when a personal or family history of epilepsy is obtained, the fits may prove to be hysterical, as there is nothing more likely to suggest a fit in response to continual strain than the subconscious fear of their occurrence in a man who has previously suffered from epilepsy or who has witnessed many fits in his near relatives. In some cases the individual continues to have occasional attacks of true epilepsy, although most of his fits are hysterical. In these the diagnosis of hysteria may be difficult, as the patient is so familiar with the characteristics of epilepsy that his fits often closely simulate true epileptic attacks. Thus we have seen several cases in which during an hysterical fit the patient has bitten his tongue and passed his urine, two symptoms which are very familiar to every epileptic. A diagnosis can often be made by the patient's behaviour in the middle of the fit, a period in which the complete absence of consciousness in true epilepsy prevents the sufferer from being familiar with what actually occurs. Thus in the hysterical fit he often struggles with onlookers and clutches at neighbouring objects; he rarely appears to be completely unconscious, and there is no conjugate deviation of his eyes. The most conclusive signs, however, are those which are beyond the control of the individual, such as cyanosis in contrast to the congestion or pallor in hysteria, and the extensor plantar reflex, often present at the end of a true epileptic attack, but never in hysteria.

I believe that these considerations are applicable to the epilepsy of civil life, and many individuals, particularly among those who are not of a neurotic type, have been labelled as epileptic and have for years been drugged with bromides, having their whole outlook on life embittered, when they could have been cured completely by psychotherapy. In many other cases, in which epilepsy and hysteria coexist, the majority of the attacks could be prevented by psychotherapy according to the mehods described by Captain R. G. Gordon (5), whilst the true epileptic fits could be controlled by small doses of bromides given at the proper time.

In most accounts of epilepsy it is said to be possible to prevent the development of an attack beginning with a peripheral aura by tying a ligature or applying a blister above the affected part. I have myself described a case of this kind and have thought that a spray of ethyl chloride to the epigastrium, when this was the seat of the aura, has prevented the fit developing. But the aura depends on changes in the brain and not in the periphery, and I now realise how inconceivable it is that anything done at the periphery could affect the fit which follows, unless the fit was hysterical, when the manœuvre would act by suggestion. It would be as reasonable to expect that a ligature round the ankle of an amputated leg could influence the sensation of tingling in the toes, which is occasionally felt as a result of irritation of the nerve-endings in the stump. A history of the successful arrest of fits by means of this kind should therefore be taken as an indication that they are hysterical.

The result of the administration of bromide in a case of supposed epilepsy does not greatly help in the diagnosis, as it is by no means always possible to prevent true epileptic fits with bromides, and if taken by the patient with sufficient conviction, bromide may sometimes stop hysterical fits by suggestion, and it is perhaps in cases of this kind that borax and belladonna, which have been highly recommended by some physicians, though found useless by most, have proved successful.

It is certainly difficult in a crowded out-patient department to obtain a sufficiently accurate history to make a definite diagnosis between true epilepsy and hysteria, especially as an actual fit is only seen in a small proportion of cases, and even if one is seen it does not follow that all are of the same nature. I am convinced,

however, that more care should be taken in coming to a conclusion than is generally the case, and that the possibility should always be considered, however little the patient corresponds to the popular conception of an hysterical individual.

Hysterical Tremor. Until recently the view taken by Meige in France and Oppenheim in Germany that the tremor in soldiers is an emotional neurosis, which differs from hysteria in not being amenable to psychotherapy, has been widely accepted. Meige had himself pointed out that the tremor was always accompanied by rigidity, and assuming that it could not exist without the latter, we attempted to cure it by inducing complete muscular relaxation by persuasion and re-education. We found it possible in this way to relieve at a single sitting the severest tremor in soldiers, whether universal or confined to one or more limbs, or to the head, jaws, or eyelids. The condition originates as a natural response to the emotion of fear, and is perpetuated by auto-suggestion when the fear is no longer present; it is thus a genuine hysterical symptom.

The nightmares, depression, and headache frequently associated with tremor disappear as soon as the latter is cured, although some cases require further treatment by psychotherapeutic conversation and hypnosis. The principle of treating the associated rigidity in order to relieve the tremor should prove of value in dealing with some forms of tremor in civil life.

Tics. During the first three years of the war we treated tics by the methods introduced by Meige and other French neurologists, in which the patient is taught to control them by voluntary effort. But improvement was slow and uncertain, as it is in civil practice, so we were glad to be able to apply to tics the lessons we had learnt in dealing with hysterical tremors. The result was very satisfactory, and we have seen no case of a tic in a soldier which did not rapidly respond to direct psychotherapy. We found that the symptom invariably resulted from the perpetuation by auto-suggestion of an act which originally had a purpose, but continued when this no longer existed. A tic thus falls within the definition of hysteria, and I can see no reason for regarding it any longer as a distinct functional nervous disorder. The mental attitude, which Meige described as characteristic of a man with a tic, is certainly not always present, and it is doubtful whether what he regarded as the psycho-

logical basis of tics may not often, like the physical stigmata of hysteria, be a result of unconscious suggestion by the observer.

Facial Spasm. In cases of involuntary facial movement it has long been customary to consider the possibility of hysteria, tic, and true facial spasm. As I have just pointed out, a tic is probably nothing else than hysteria, and I now recognise that many cases which I formerly would have regarded as examples of true facial spasm, in which the pathogenesis was obscure and the treatment very unsatisfactory, were really due to hysteria. Babinski taught that in organic facial spasm all the muscles of the face contracted, just as if the facial nerve were stimulated, whereas in hysteria the corrugator supercilii, for example, did not contract with the orbicularis palpebrarum, and the only muscles which took part were those which a man would use if he voluntarily screwed up his face. But we have seen several cases of facial spasm in soldiers in which every muscle took part, including in one instance even the extrinsic and intrinsic muscles of the ear, which the patient had never been able to contract voluntarily, although the condition was clearly due to auto-suggestion and was cured by psychotherapy. It follows that if there is no evidence pointing to any organic source of irritation of the facial nerve, facial spasm should be regarded as hysterical and psychotherapy attempted, as there are no physical signs by which hysterical facial spasm can be distinguished from spasm of organic origin.

Stammering. For a long time we regarded the stammering, which is a common symptom in soldiers, as a condition requiring prolonged re-education, the only method employed with any success for the stammering of civil life. But improvement was slow and by no means uniformly good. When at length we recognised the hysterical nature of the tremor of soldiers and how quickly it could be cured by psychotherapy, we wondered whether perhaps stammering should not be regarded as a kind of hysterical tremor of the muscles involved in speech, associated with a spastic condition of the respiratory muscles, which could be rapidly cured by methods analogous to those used for tremor in other parts of the body. As our confidence in psychotherapy increased, we became increasingly successful, until now we can almost invariably cure a war stammerer at a single sitting, often so completely that he can speak in front of a class of medical officers

without hesitation, although before he may have been almost completely unintelligible even with his friends. From a very limited experience with children since we recognised the true nature of stammering in soldiers, I believe that all stammering will eventually prove to be hysterical, and that in children it will be possible to cure it rapidly. Even in adults it should often be cured in the course of a few sittings, if the physician can convince himself and his patient that this is the case, instead of holding the view that rapid recovery is impossible and that the best that can be expected is very slow improvement with prolonged and painstaking re-education.

Vomiting. Our war experience, which has recently been summarised by Capt. W. R. Reynell (6), has shown that hysterical vomiting is extremely common. The suggestion which gives rise to it is always the vomiting due to some other cause than hysteria. In every case of vomiting auto-suggestion may lead to the symptom being perpetuated after the primary cause has disappeared, or to its being aggravated by auto-suggestion whilst the primary cause is still present.

Vomiting may be caused by direct irritation of the stomach, or it may be of psychical, reflex, or toxic origin. The first of these has been the most common cause in soldiers, the source of irritation being generally mustard gas. Whenever vomiting continues for more than a month after gassing it is invariably hysterical. Analogous to this is the vomiting of civil life, which begins with an acute attack of gastritis and continues after the irritant which caused it and the actual inflammation has disappeared. Much of the continued and cyclical vomiting in children is probably of this nature, the symptoms which are supposed to point to the presence of toxæmia being in most instances simply the results of starvation. Anæsthetic vomiting is primarily due to irritation by swallowed ether, but in patients who have ever vomited after an operation, every subsequent anæsthetic is likely to cause vomiting, which can often be prevented by a few preliminary words of encouragement, as the condition is largely hysterical.

We have seen several cases in which the onset of vomiting in soldiers dated from some particularly disgusting sight which led to continual vomiting. An unpleasant emotion is a common cause of vomiting in women, in whom certain acts or sights, recalling the

primary emotional origin, continue to give rise to vomiting, until the cause is explained, when recovery quickly follows. The wife of an officer vomited for the first time in her life on accompanying him in the train at the end of a short leave in the second year of his services abroad. After this she continued to vomit whenever she travelled or found herself in a confined space, so that she could not enter any vehicle or go to church or to a theatre. After continuing for over two years the symptoms ceased abruptly when the cause was explained to her.

Reflex vomiting, due to such organic conditions as chronic appendicitis or phthisis, is often exaggerated by auto-suggestion; we have seen several soldiers who had been vomiting after every meal as a result of these conditions, but who vomited only at very rare intervals or even ceased to vomit at all as a result of psychotherapy. The vomiting which may persist after the removal of an appendix is of the same nature, and I believe that many of the cases of intractable vomiting after abdominal operations, in which no cause can be found at secondary operations or even after death, are hysterical and could be cured by psychotherapy.

The very common vomiting in young anæmic women is generally hysterical, as it is at once cured by persuasion and re-education if a full diet is given, even if the patient has lived on slops for months. Two years ago I saw a nurse who had vomited everything for three months, and for four weeks had been on rectal feeds with no improvement. An operation was contemplated, but I explained things to her and ordered her a good dinner, which she kept down, and she never vomited again. Whether the vomiting in these cases is primarily due to irritation, reflex action from the bowels or elsewhere, or toxæmia, I do not know, but its immediate cessation with psychotherapy proves that it is ultimately hysterical.

The so-called pernicious vomiting of pregnancy is always, so far as my limited experience goes, hysterical. The symptoms which are supposed to indicate the presence of toxæmia are, I believe, a result of starvation. If this were realised the lives of many mothers and of a still larger number of infants would be saved, as it should never be necessary to induce labour for this condition, which can easily be cured by psychotherapy.

It is even possible that the ordinary vomiting of pregnancy is

often hysterical. Every woman knows that she is likely to vomit when she becomes pregnant, and the presence of other evidence of pregnancy may suggest vomiting. The fact that a woman has vomited at her first pregnancy is likely to suggest vomiting at subsequent pregnancies. Whenever the early vomiting in pregnancy is very troublesome, the possibility of relieving it by psychotherapy should therefore be considered.

I dedicate this paper to Sir William Osler as a token of affection, admiration, and gratitude. To his advice, his encouragement, and his teaching, I owe a debt I can never repay.

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CHRONIC TUBERCULOSIS OF THE CHOROID

By Edward Jackson, M.D., Denver, Colo.

THE ophthalmoscopic picture of early or acute tubercle in the choroid has been known for fifty years, and often described and represented. But it has commonly been recognized in the later stages of acute tuberculosis or tuberculous meningitis, when the death of the patient soon cut short the evolution of the lesion. Hence, the familiar picture of this condition is simply that of a small, light-yellowish spot in the fundus, rounded or oval in form, commonly less than one-half millimeter in its greatest diameter, with an indefinite edge. It is the picture of a mass of choroidal exudate without visible alteration in vessels, or pigmentation, or signs of atrophy. Such acute lesions may become strikingly evident in a few hours.

In the last ten years the existence of a chronic tuberculosis of the choroid has been generally recognized; but the descriptions of its early evolution are still deficient and fragmentary. The account here given is based largely on the case that is here outlined, which has been observed by the writer under peculiarly favorable conditions, and over a period of about eight years.

Case. May 25, 1911. G. M. H., aged twenty-two, came with a history of eye strain and headache, relieved by wearing R.+0.50 cyl. axis 120°; L.+0.37 cyl. axis 90°, which had been given her a year ago. Last September she noticed a central scotoma in the right eye, which appeared suddenly and grew larger, with "dazzling" of that eye. The eye conditions puzzled the physician and oculist in charge. It was not recognized to be tuberculous. But her working as a stenographer being interdicted, she came from Pittsburgh, Pa., to Denver, Colo.

Her vision had remained unchanged for several months; R. 4/45, L. 4/3 partly, accommodation 11 D. in each eye. The ophthalmoscope showed slight pallor of the outer quadrant of the optic disk, and in the macula a nearly circular patch of atrophy of the choroid, with pigment massing, having a diameter about two-thirds that of the optic disk. Other portions of the right fundus and that of the left eye appeared normal.

Her condition remained unchanged for sixteen months, while she was doing office work with a moderate amount of stenography and reading.

September 30, 1912. She complained that for a day or two there had been some extension of her old scotoma, toward the temporal field and downward. Vision in this eye was reduced to 2/45; more distinctly excentric than it had been, fixing below the letter to be seen. With the ophthalmoscope no change in the fundus was perceived.

October 2, 1912. R. is now painful. She has noticed glaucoma haloes around the light. Tension, fingers, +T.1, Gradle tonometer. R. 2 to 3 (=60 mm. Hg.) L. 11 (=20 mm. Hg.) R. pupil slightly larger than L. The ophthalmoscope shows haziness of the fundus to the upper nasal side of the old choroidal atrophy. From this time the ophthalmoscopic changes ran the course to be presently described. Under pilocarpin, the tension of R. remained about 50 mm. for one week, but dropped to 28 mm. on October 14th, and soon to 20 mm.

For several weeks she had felt some pain and soreness about the metatarsal-phalangeal joint of the right great toe. Careful examinations revealed no pulmonary lesions. But injection of old tuberculin caused a distinct general reaction, with increased clouding in the retina and of vision of R. and increased pain in the great toe. She was put on injections of tuberculin. The choroidal condition passed slowly into atrophy, with pigment massing. The patch now involved extended nasally from the original patch, and had about four times the original area. The optic disk showed increased pallor of the temporal quadrant. She continued to work as a stenographer, gradually coming to work hard and full time.

September 6, 1918. Last April she became ill with a tuberculous pleurisy; and has been in bed since. In June, 2 quarts of fluid were drawn from the right chest, and the same amount in July. Since then she has been improving, but her temperature still rises 1° to 2° F. in the afternoon.

Four days ago she noticed an extension of the scotoma upward and to the nasal side. The ophthalmoscope shows an area of haziness on the lower temporal margin of the old patch of choroidal atrophy.

September 13. The region of retinal haze is rather larger. Tension +T. 1; pilocarpin is again prescribed.

September 20. The area of haziness is not any larger. Tonometer R. 5 (=47 mm.)

September 27. The retinal haze is much less, slight pigmentation begins to show in the recently involved area. The condition is now as shown in the accompanying colored plate. Tension 10 (=24 mm.)

October 23. Traces of haziness are now confined to the lower temporal edge of the affected area.

March 29, 1919. Tension R. 10 (=24 mm.) L. 9 (=28 mm.). The appearances of the lower part of the macular area resemble those of the other portions of the atrophic area. The optic disk is about the same as after the first extension, or as shown in the plate. The left eye has remained normal throughout.

Course of the Ophthalmoscopic Changes. When this patient had her first extension of the choroidal lesion, she was working in my office, and was frequently examined. During her second relapse she was also examined many times. The courses of the ophthalmoscopic changes in both attacks agree closely with those observed in other cases, and are as follows:

The first symptom noticed (the lesion being macular) was impairment of vision, the ophthalmoscope showing no change. Then in a few days there appeared a faint haze of light-gray color, without definite boundaries, which became lighter and more saturated with gray, until it reached its maximum in less than two weeks from the first impairment of vision. After this it became rather darker and varied toward a brownish gray.

After three weeks it began to show noticeable evidences of pigmentation, at first quite diffuse, and then massing in many discrete dots. These became more pronounced, and fewer in number, gradually shifting into marked brown or almost black patches, while the spaces between them became yellowish-white and pure white. The indefiniteness of the edge very gradually gave place to the sharp, pigment-bordered edge of the choroidal atrophy.

Soon after the pigment first appeared it showed a disposition to arrange itself in rings or ovals, inclosing lighter or more gray areas, having the familiar shape and size of acute choroidal tubercles, but these areas never became a striking feature in the ophthalmoscopic picture, and were generally difficult to recognize. Three of them are represented in the colored plate in the recently involved area, below and to the left.

The small rhomboid atrophic area, separated from, and below the main area of atrophy, appeared prior to September, 1918, during a period when she was not under observation, and without marked ocular symptoms. Slight changes in it, after it was first observed, seemed to indicate that it arose during the period of the pleurisy.

Chronic Tuberculosis of the Choroid, Showing Active and Permanent Lesions. (*Jackson.*)

The final result of this process is an ophthalmoscopic picture conforming closely to that of an area of choroidal atrophy, as recognized since the early clinical use of the ophthalmoscope. It is devoid of choroidal vessels, and but few retinal vessels are seen passing over it.

It seems probable that the marked yellowish, rounded spots surrounded by nearly normal fundus of acute choroidal tubercle arise in a period of greatly lowered body resistance to tubercular invasion. With better resistance, the tubercle is hidden by a cloud of retinal exudate, until, as the process subsides, it is destroyed. Under the latter condition in the choroid it probably never reaches the stage of a central avascular, cheesy mass.

The choroid is little more than a mass of blood vessels, and, except in patients who have reached the depressed condition that invites general miliary tuberculosis, it is able to prevent the full evolution of the tubercle, although in the end these vessels are destroyed in the contracting scar tissue. The rare exception to this rule is seen in the few cases of chronic tuberculous masses—conglomerate tubercle—and these masses may start in ocular tissues other than the choroid.

During the early stages of these tuberculous invasions, the general appearance of the choroid was rather dark, "red and patchy," much as it may appear in cases of marked eye strain. It is possible that a choroidal congestion, such as this appearance indicates, may be the basis of the increased intraocular tension; which, in my experience, generally arises early in chronic uveal tuberculosis.

THE INTIMATE RELATIONSHIP OF CHOREA, RHEUMATISM, AND CARDIAC DISEASE

By Henry Koplik, M.D., New York

INTERWOVEN in the inspiring life work of William Osler, the physician, will be found the most interesting reflections upon the relationship of chorea and rheumatism, with remarks upon the existence of endocarditis in the former disease. In fact, to the writings of Osler we owe a modern revival of interest in this most important theme of medicine.

The pediatric physician is strongly impressed with the fact that chorea is a very serious affection, in that one attack by no means confers an immunity, as it does in some infectious diseases, from subsequent recurrences of the disorder. I feel that once a child is attacked with chorea we must always await with suspense a subsequent attack. In fact, of 319 cases of chorea in my own hospital, 104 had more than one attack, and some children actually had four and five attacks. It is unusual to find a patient who has had an attack of chorea free from recurrent attacks.

In his early work upon chorea, Osler called especial attention to and laid stress upon the occurrence in these individuals not only of manifestations of rheumatism, but cardiac disease. The functional murmur, so called, could be seen in the course of time to develop into the well-recognizable cardiac valvular lesion. The so-called functional murmur of the heart in chorea must be looked upon with a certain degree of disquietude. In the discussion upon chorea before the American Pediatric Society in 1892, Osler remarked "that of 110 cases of chorea 54 had organic disease of the heart. . . . There is no other disease in which endocarditis is known to be so frequently associated, and no other disease in which post-mortem records show such a large proportion of endocarditis."

The percentage of occurrence of rheumatism in these cases approaches the English statistics quite closely. In my own experience, that of a lifetime in the medicine of pediatrics, I find a very

serious indication that chorea, rheumatism, and cardiac disease are very closely knit into a composite picture. I have watched cases of chorea with recurrent attacks to find after years a fully developed cardiac lesion where at the start none existed, though the manifestations of rheumatism were present.

What are the literary records in this disease? Among the English writings none is more respected than are the observations of Gowers. This classic writer, after quoting Hughes and Germaine Sée, says that in one-fourth of his cases rheumatism or a history of such was present, varying at different ages. He says: "The proportion in late childhood is too large to be a matter of accident. Chorea follows rheumatism and the latter frequently follows in the course of chorea, and by the mysterious and unquestionable relationship of chorea and heart disease."

Here let me call attention to the fact that the term rheumatism should include not only the acute rheumatic attack with fever, pain, and swelling, but the so-called rheumatic pains and the "growing pains," as pointed out by early writers (Jacobi), are as truly rheumatic in children as the fully developed rheumatic fever with joint swellings.

Cardiac disease may gradually develop in children who for months or years complained simply of rheumatic pains in the various joints, but who finally presented a fully developed cardiac lesion with all the concurrent symptoms of heart disease. Goodheart and Still mention that in 141 of their cases 39 had rheumatic fever and 50 had a history of rheumatism in near relatives. "In many cases the chorea is the first symptom of rheumatism and the further evidence of chorea appears later." Thomson says, "Chorea is not seldom the first of a series of rheumatic phenomena." Again, in another place he says, "in a considerable proportion of cases chorea is beyond all doubt a manifestation of rheumatism."

Among the English writers the so-called rheumatic nodules, which with us in America are not so common a manifestation of rheumatism in chorea, are widely quoted in support of the rheumatic theory of chorea and as a support of its close association with rheumatism. Still says that, of 388 cases of chorea, 183 had concurrent or previous articular rheumatism (pains in limbs or joints), with or without heart affections and nodules; 8 had no joint

symptoms, but had heart disease and rheumatic nodules; 2 had rheumatic nodules without cardiac bruits or joint symptoms; 12 had systolic and diastolic apical bruits; 3 had aortic diastolic as well as apical bruits, and 48 had systolic apical bruits without joint symptoms or nodules. At the very lowest estimate 54.3 per cent of the cases which came under treatment for chorea showed positive evidence of rheumatism.

It is needless to multiply quotations from the literature in support of our theme. It would only add support to the feeling that chorea is a rheumatic manifestation of rheumatic infection, and eventually unfolds the symptom complex of rheumatism, including an involvement frequently serious and fatal, of the cardiac structure. I have collected from my hospital experience statistics of 319 cases of chorea, all studied most carefully as to the relationship of rheumatism to this affection. These cases occurred in the course of ten years and were consecutive cases. They were of all degrees of severity, and 13 of them advanced to the stage of absolute paralysis, that is, the children lay in chorea and absolutely helpless, unable to raise limbs or to talk or respond to volitional impulse. Some of these cases were for months under hospital observation, so that there can be no doubt as to the constant daily notation of symptoms. Of these cases we were able in only 8 to establish a family history of rheumatism, and this to my mind would rather disprove than support any theory as to congenital or familial nature of rheumatism *per se*. As to the presence of rheumatic symptoms in the *patients themselves*, I was able to establish a positive history of rheumatism, either rheumatic pains or articular attacks, in 46 cases, or 14 per cent. This corresponds quite accurately with Osler's statistics of 15.8 per cent. From this it will be seen that, in considering large numbers of children who suffer from chorea, the rheumatic tendency with its symptomatology is easily discoverable, to say the least. When we turn to another aspect of the symptomatology as regards the heart structure, there is still striking, conclusive evidence that whatever the poison at the bottom of the etiological causation of the disease, there is a menace to the heart in an overwhelming majority of the cases. It is not uncommon to see cases of chorea in the first attacks free from cardiac disease. In subsequent attacks the cardiac lesion will develop and finally the patient may become

a cardiac sufferer without chorea symptoms. Of the sum total of 319 cases of chorea in my statistics, 232 showed undoubted cardiac disease, the result of endocarditis.

Here let me remark that as patients come into the hospital they may show cardiac lesions and chorea, but no temperatures. That is, they have no signs of active acute endocarditis. This is quite characteristic of chorea. There is little or no temperature during the whole course of the choreic symptoms. It is difficult to conclude as to the possible presence of temperature at times when this temperature was unobserved. I am fast coming to the conclusion that there are cases of rheumatic endocarditis, especially in chorea, which run a course without any marked rise of temperature, certainly not a rectal temperature above 100.5°. This is quite characteristic of chorea. In other words, chorea and endocarditis without temperature are not incompatible.

CHOREA

Ten consecutive hospital years

Ages, Years	Cases	Rheumatic	Cardiac
4–12	29	7	28
4–13	25	2	20
3–14	34	7	29
4–13	30	6	23
3–13	46	4	27
2–16	30	4	24
5–12	23	2	22
5–13	38	5	19
4–12	33	6	17
4–12	31	3	23
	319	46	232

Recently I have been impressed with cases of children who apparently are rheumatic with rheumatic joint pains, who after years develop heart lesions. They are rheumatic, and never have any outspoken rheumatic fever, nor do they have joint swellings and still develop serious heart lesions. In these cases I am well aware that the children may have had attacks of fever of short duration, diagnosed as grippe. Yet granting this, there has been no so-called rheumatic fever of any duration; so in chorea there is a gradual development of cardiac lesions without marked febrile course, and this is quite characteristic of chorea, and has not been sufficiently commented upon hitherto. Another fact which becomes apparent

in the study of my statistics is that in an overwhelming number of cases the cardiac lesions developed in what was said to be the first attack of the disease. Quite significant is the fact that of the 232 cases of chorea which showed cardiac disease 155 developed the lesion in the first attack of chorea; that is, 50 per cent of the cases. In fully half valvular lesions developed in the first attack.

Therefore, in fully 50 per cent of the cases of chorea in which cardiac lesions develop, the lesions appear in the first attack. In 72 per cent of the cases (232 of 319) heart lesions finally developed. In a convincing proportion of cases rheumatic symptoms are apparent.

It is true that rheumatic manifestations are common to many acute infections, but the accompaniment of heart involvement in chorea with rheumatic manifestations must leave us to conclude that chorea may eventually be proven to be caused by some infection closely allied to that of acute articular rheumatism.

RESPIRATORY SYMPTOMS DUE TO LATENT SYPHILIS

By H. R. M. Landis, M.D., Philadelphia

Assistant Professor of Medicine, U. of P.; Director of the Clinical and Sociological Departments of the Phipps Institute; Visiting Physician of the White Haven Sanatorium

DISPENSARIES and hospitals dealing with the care of tuberculous individuals receive during the course of a year a very considerable number of patients who are either not tuberculous or in whom a diagnosis of tuberculosis is open to doubt. Frequently the patient is referred to the dispensary or sanatorium by a physician; again the patient, because of more or less marked respiratory symptoms, seeks medical advice on his own initiative. The problem in all instances, especially as regards the dispensary, is to establish, in so far as it is possible, a definite diagnosis. For some years the criticism has been made of dispensaries and to some extent of sanatoria, that they carry on their lists many patients in whom the diagnosis of tuberculosis is questionable. It is desirable that the diagnosis should be open to as little doubt as possible, not only on account of the patient's peace of mind, but also for economic reasons. It is quite apparent that individuals who do not suffer from tuberculosis or those who harbor old, arrested lesions should not be subjected to sanatorium treatment, as they not only cause the State needless expense, but in addition confuse our notions of both the frequency and the curability of tuberculosis.

If the dispensary is to carry out properly the function of a clearing house, each case must be carefully studied. The one factor which places the diagnosis of tuberculosis beyond question is the presence of tubercle bacilli in the sputum. Such a finding establishes the diagnosis beyond a question of a doubt. Unfortunately this group of cases is made up for the most part of the far advanced and the moderately advanced type of the disease, in which the symptoms, physical signs, and course of the illness make the etiology

reasonably certain. The real trouble is in dealing with that group in which the symptoms range from those suspiciously tuberculous in origin to those almost certainly so, but in which the physical signs are inconclusive and tubercle bacilli are absent. The number of patients in this group who finally will be designated as tuberculous will depend largely on the policy of the particular institution. In one a liberal attitude will be taken and the number of positive diagnoses will be correspondingly large; in another a spirit of skepticism prevails with a correspondingly small number of positive diagnoses.

In studying patients who are not definitely tuberculous, many can readily be shown to be suffering from some well-recognized lesion of the lungs, pleura, or heart. But after we have eliminated those in whom the respiratory symptoms are explainable by reason of the history, the location of the lesions or the bacteriological findings, we are still confronted with a considerable number in whom it is often difficult to give a definite opinion. In this group the symptoms are usually strongly suggestive of pulmonary tuberculosis. The physical signs may be typical of those encountered in tuberculosis, but often abnormal physical findings are absent or very slight in proportion to the severity of the symptoms. The discovery of the etiological factor is the all important thing in this group. If the examination of the sputum repeatedly fails to show the presence of tubercle bacilli, careful search should be made for one of the mycotic organisms. If the latter can be ruled out, a chronic inflammatory condition probably exists. The etiology of these conditions is often difficult to establish. Fibrous tissue can arise from such a variety of causes that it is not easy to determine in its final stage what the initial process was. Among the possibilities is syphilis.

Even before the discovery of the *Spirochæta pallida*, and later the introduction of the Wassermann test, it was universally recognized that syphilis was one of the most protean of all diseases. It was generally admitted that it might exist in a latent form for years and from time to time manifest itself, sometimes in the guise of other diseases, in other instances by obscure symptom complexes. To such an extent was this true that it has been traditional for years that in all obscure conditions syphilis is always to be thought of as the possible etiological factor. Medical literature abounds in

instances in which the acting on such a suspicion has resulted in the most brilliant therapeutic results.

It is hardly necessary to recall the conditions which have always been regarded as being probably syphilitic in origin, namely, general paralysis of the insane, tabes dorsalis, thoracic aneurysm, etc. We now possess the knowledge that makes it possible to remove these conditions from the class of probable manifestations of syphilis to that which is certainly luetic in origin. In other instances, syphilis is believed to be the exciting factor, although the final result differs in no particular from that produced by other etiological factors.

So rapidly has our knowledge of syphilis been extended since Schaudinn's momentous discovery and Wassermann's introduction of the complement fixation test, that one is probably safe in saying that there is no tissue of the body which is immune to its ravages; and although we lack the specific proof that this is true in every instance, enough has been done to make it highly probable that ultimately the final demonstration will be supplied.

Among the viscera which are regarded as especially resistant to syphilis are the lungs. Prior to the discovery of the tubercle bacillus, pulmonary syphilis was regarded as being relatively frequent, and the older literature contains numerous references to the subject. After the discovery of the tubercle bacillus and the clarifying of our views as to the lesions produced by this organism, it became apparent that many of the cases reported as being examples of syphilis of the lungs were in reality tuberculous in nature. There then followed a period in which the diagnosis of pulmonary syphilis was rarely made, and indeed up to the present time such a diagnosis is regarded with a certain degree of skepticism. This attitude has been brought about almost entirely by the pathologist, who demands the etiological or anatomical proof. Fortunately or unfortunately, as the case may be, the majority of the clinical observations have resulted in cures, and therefore, aside from the Wassermann reaction and the therapeutic test, other proof is, as a rule, wanting.

Several years ago our attention at the Phipps Institute was directed to syphilis as the possible cause of respiratory symptoms in patients in whom it was impossible to establish a definite diagnosis

of tuberculosis. These observations were recorded in a paper by Lewis and myself.[1] It is significant that of the six cases recorded by Lewis and myself three had spent some months each at a tuberculosis sanatorium, and of the cases reported below two were subjected to this treatment.

Our belief that syphilis of a latent type might be the cause of persistent respiratory symptoms arose from the fact that patients were occasionally encountered in whom the symptoms and physical signs were strongly suggestive of tuberculosis, but in whom neither the tubercle bacillus nor other less familiar organisms could be demonstrated. Furthermore, the Wassermann reaction was strongly positive, and in addition some of them had well-marked syphilitic stigmata. Since that time we have continued these observations: (1) by a more extended application of the Wassermann test and (2) by a routine examination of all patients for possible syphilitic stigmata.

As a result of our observations during the past two or three years we have encountered the following examples of what we believe to represent a latent type of syphilis which manifests itself chiefly by respiratory symptoms.

Case I. (Phipps Institute No. 15,263.) Male, white, age fifty-seven. He gave a history of having had a chancre in his youth. Eight years prior to being seen at the dispensary, he had an attack of pleurisy at the right base (probably a perihepatitis). He gave a history of having had a cough with whitish expectoration for one year. During this time his weight had fallen from 198½ to 160½, and for the past eight months he had been unable to work. He had an irregular type of fever ranging from normal to 100° F.

Physical examination showed some flattening beneath the right clavicle with impairment of the percussion note both anteriorly and posteriorly over the right apex. The breath sounds were broncho-vesicular in character over this area and posteriorly fine submucous râles were heard. An *x*-ray examination of the chest showed the presence of some connective tissue at the base of the right lung. This extended upwards along the bronchial trunks. In addition there was a diffuse shadow over the right upper lobe which obscured the lung details. The aorta was tortuous.

Because of repeated negative sputum examinations and a plus 4 Wassermann, the patient was placed on antisyphilitic treatment. In a

[1] *Am. J. M. Sc.*, Aug., 1915.

few weeks he began to gain in weight. The respiratory symptoms gradually disappeared, as did also the râles at the right apex. In the course of two months he resumed his work. When last seen he was free from symptoms and his weight was 195.

Case II. (Phipps Institute No. 16,817.) Female, white, age twenty-four. Married, two miscarriages—one child died of hereditary syphilis. She gave a history of having had pain in both sides of the chest, cough, and expectoration for two and a half years. On several occasions her sputum was blood-streaked. For the past two years she had some dyspnea and for two months hoarseness. Her weight had fallen from 116 to 76 pounds.

Physical examination showed the presence of numerous asthmatic râles throughout both lungs. She was sent to a tuberculosis sanatorium by a social agency and remained for several months; during this time she regained some weight. The diagnosis at this institution was "advanced tuberculosis" in spite of the fact that her sputum was negative for tubercle bacilli. On her return to the Phipps Institute her Wassermann was found to be plus 4. This fact and the history of two miscarriages led to the giving of antisyphilitic treatment. As a result of a course of treatment with salvarsan her pulmonary signs disappeared entirely, she gained in weight, and at the present time presents every appearance of being well.

Case III. (Private patient.) Female, white, married, age twenty-eight. This patient requested an opinion as to whether she had tuberculosis. She stated that she had suffered from respiratory symptoms off and on for eight years and that on two occasions, for periods of four months each, she had been sent to a tuberculosis sanatorium. Her trouble had started eight years ago with a severe cough and expectoration which lasted for eight months. Two years ago she had what she described as "three touches of pneumonia." During this entire time she had never been entirely free from cough. Her expectoration was often blood-tinged and at times she had some fever; at present she tires easily. For the past four years she had been troubled with nasal catarrh and slight deafness.

Physical examination. The patient was a well-nourished woman. Aside from a suspicious flattening of the bridge of the nose nothing abnormal was found. The lungs were remarkably free from any abnormality in spite of the long history of respiratory trouble. Fluoroscopic examination of the chest showed nothing abnormal. The fact that she had left her husband because of his dissipated habits, and the history of probable gonorrheal salpingitis, suggested the possibility of a luetic infection also. Additional factors were the deafness, nasal catarrh, and the flattening of

the bridge of the nose. The Wassermann reaction was plus 4, and repeated examinations of the sputum have failed to show tubercle bacilli.

Case IV. (Phipps Institute No. 15,652.) Female, white, married, age thirty-nine. One still-born child. Had suffered with dyspnea for two years. For four months had had hoarseness, cough, and yellow expectoration. Since the onset of her illness she had lost 22 pounds in weight. During the time she was under observation she had slight fever of an irregular type.

Physical examination showed some impairment of the percussion note, broncho-vesicular breathing and fine râles at the right apex. The sputum was negative for tubercle bacilli, and the Wassermann reaction plus 4. Under antisyphilitic treatment (mercury and iodide) the symptoms disappeared, the physical signs cleared up and she gained 21 pounds in weight.

Case V. (Phipps Institute No. 16,365.) Male, negro, married, age thirty-five. When first seen he gave a history of having had a cough and expectoration and pain below the left scapula for one year. Had also had considerable dyspnea for eight months. During this time he had lost 22 pounds in weight. The sputum did not contain tubercle bacilli and the Wassermann reaction was plus 4.

Physical examination showed the presence of subcrepitant râles at the bases of both lungs. Under the use of antisyphilitic treatment (mercury and iodide and later salvarsan) he regained the 22 pounds loss in weight and showed marked improvement in both the symptoms and physical signs.

In submitting these cases as examples of pulmonary syphilis, I clearly realize that the absolute proof demanded by the pathologist is lacking. On the other hand, these patients responded as readily to antisyphilitic treatment as do those suffering from luetic lesions in other portions of the body—the etiology of which is beyond cavil.

In the series of cases here presented as well as in those detailed in our previous paper, it is evident that we have to deal with instances of disease marked predominantly by respiratory symptoms. The constitutional effects are by no means trivial, in fact have been profound in several instances. The physical signs and the results of *x*-ray examination have frequently shown the existence of diffuse or localized lesions of some degree of severity. Serum examination has revealed a positive Wassermann reaction. The cases have been much improved or even apparently cured by antisyphilitic treatment.

The results of the Wassermann reaction and the response to treatment render it probable that the cases are syphilitic in origin. It is, of course, true that the examination of the chest has revealed no lesions of this type, or of the severity ordinarily recognized at the post-mortem table as syphilis of the lung. It seems not improbable that lesions of pulmonary syphilis other than the classical may exist. In view of the frequency with which the mucous membranes of the mouth, naso-pharynx, and larynx become ulcerated in syphilis, it is certainly not improbable that a syphilitic bronchitis may at times exist. Nor is it unlikely that patches of syphilitic pneumonia may develop either independently or as extensions from a preceding bronchial condition. If these assumptions be admitted, the syphilitic nature of these cases, and as a corollary the existence of syphilitic lesions of the lung, other than those described by pathologists, is clear.

If, on the contrary, it is held that the descriptions already furnished of syphilis of the lung are complete, then another explanation for at least a part of the cases presented is in order. In view of the positive Wassermann reaction and the response to treatment, it would be logical to assume that we have to deal with some form of spirochæte infection other than syphilis. French and Italian observers recognize a form of spirochætal bronchitis, but it is not known to exist in America. It must be acknowledged that such an explanation of these cases is possible. In its favor perhaps may be the fact that certain of these cases have yielded to treatment with ease. Syphilis of the mucous membranes is also easy to cure. It is, however, as a rule, very difficult to secure permanently negative Wassermann reactions in late syphilis, and this seems to have been the result in certain of these cases, although the period of observation is still too short to enable one to speak with finality on this point.

HEREDITARY HEMOPTYSIS

By E. Libman, M.D., and R. Ottenberg, M.D., New York

(From the first Medical Service of Mt. Sinai Hospital, New York City)

As our knowledge of the subject increases, the group of hemorrhagic diseases is constantly being subdivided into new clinical and pathological entities. Even in the group of characteristically hereditary hemorrhagic diseases, there are at least two absolutely distinct conditions, the fairly common hemophilia with its sex-limited inheritance, and the hereditary telangiectasis of Osler with definite anatomical lesions, not sex-linked in inheritance.

On the basis of a family investigated by us in which seven bleeders presented almost identical histories, we believe that we are warranted in describing a new clinical type of hemorrhagic disease. Whether further investigation will prove this to be a variation of multiple telangiectasis or to be an independent condition, we are as yet unable to decide. As will be noted in the clinical histories to follow, telangiectases could not be demonstrated after careful search, the trachea and bronchi being also examined in two instances.

The first member of the present family to be seen by us was admitted to Mount Sinai Hospital while suffering from profuse hemoptysis. It developed that he had suffered from similar attacks at intervals for many years. Naturally, he had been repeatedly suspected of being a victim of pulmonary tuberculosis, but no proof in favor of such a diagnosis had ever been obtained. He had never suffered from any other symptoms except the hemoptyses themselves. Furthermore, upon investigation, it was found that six other members of the family (two of whom were examined by us) gave practically identical histories—numerous hemoptyses commencing in adult life, and not interfering with the general health. There were no cases of tuberculosis in the entire family, and none of the family were bleeders in any other sense; that is, none of them

bled inordinately from accidental wounds or otherwise than from the lungs.

Careful examination of the blood of the patient admitted to the hospital showed that it lacked the characteristics of hemophilia: the coagulation time was normal. The characteristics of chronic purpura were also absent; the platelet count was within the normal range, and the bleeding time was normal.

The heredity of the disease in this family is not sex-limited, the disease occurring in and being transmitted by females as well as males. The hemorrhages occur only at or after the age of puberty, the earliest hemorrhage recorded in any individual being at the age of twelve years. None of the hemorrhages has been fatal.

Considering the possibility that the condition might be one of telangiectasis similar to those of multiple hereditary telangiectasis, but situated in the bronchial tree, we secured the kind services of Dr. Yankauer, who performed bronchoscopy on two members of the family, with entirely negative results. It must therefore be concluded that if the condition is due to telangiectases, they must be localized in the finer bronchi or in the pulmonary tissue. On the basis of physical examinations of three lung bleeders belonging to the family, as well as of roentgenologic examination of two, and tuberculin test of one, and on the basis of the clinical fact that none of the seven individuals who suffered from hemorrhages ever developed any of the symptoms of tuberculosis, we believe that tuberculosis can be excluded as the cause of the hemorrhage.

Case I.[1] R. W.; Russian Jew; jeweler; age thirty-two years; admitted to the hospital, service of Dr. Libman, October 12, 1916; discharged October 23, 1916.

Family History. Patient's maternal grandmother (1)[1] had attacks of hemoptysis exactly like those of the patient. She lived to be seventy years of age; cause of death unknown. Patient's mother (2)[1] died at sixty-six, of a sudden heart attack; was previously weakly, and had suffered from attacks of hemoptysis every few months for at least ten years. Patient's father is alive at eighty-one. Since the age of seventy he has been subject to asthma and severe coughing, and has had occasional hemoptysis (slight streaks of blood—not hemorrhages like the rest of the family). The father and mother are not blood relatives. Patient's mother had one brother and

[1] Refer to numerals in the appended family tree.

one sister. The mother's brother (3)[1] is fifty-six years of age and has been subject to attacks of hemoptysis similar to those of the other members of the family for at least twenty years. One of his sons has recently expectorated blood for the first time (see history below, III).

Patient has three brothers and two sisters, of whom one brother and one sister are subject to attacks exactly like his own. His brother (4)[1] is forty-three years of age, and is suffering from attacks which came on first during adult life. They occur at irregular intervals of a few months and have been absent as long as 2½ years. His sister is thirty years old, and has had frequent attacks since the age of twelve. A more detailed account of her is given below (II).

The patient himself has three children, aged thirteen, ten and six, respectively, who have so far not suffered from hemoptysis. There has been no case of tuberculosis in the family.

Previous History. He had typhoid fever at the age of six. Two months ago he suffered from an attack of malaria (chills and fever lasting eight days). During the attack his urine was extremely dark, but, as far as he knows, did not contain blood. He formerly had an occasional epistaxis, otherwise is not subject to bleeding, and none of the other members of the family has bled from accidental cuts longer than other persons.

Personal History. He denies gonorrhea and syphilis; uses tobacco in moderation, no alcohol.

Present Illness. Patient has been subject to attacks of hemoptysis since the age of twenty-one. During the first three years he had six attacks. Then they became somewhat more frequent. In the last five years he has bled only five or six times, the last attack occurring three months ago. He has been repeatedly examined by various physicians, and pronounced not tuberculous. The attacks almost always start when he arises in the morning. He says that he is a mouth breather and his throat is very dry when he wakes up. On this account he usually has to cough very hard every morning. The bleeding comes on only after about ten minutes of hard coughing, and he attributes it to the coughing. At the start it is usually slight, but gradually increases. At first the blood is bright red, but by the second or third day it is generally dark in color. He knows by experience that when black blood appears there is no more danger of bleeding, and returns to his work. He does not generally call a physician, as he has learned that the bleeding always stops spontaneously. According to his estimate, he loses about a half pint of blood in an average attack, but sometimes as much as a pint and a half. Except for the attack of malaria, two months ago, he never had chills or night sweats.

The present attack began ten days ago, and he is still bleeding. For

the last day the blood has been rather dark. He feels weaker at present than he usually does after a hemorrhage, and this is what led him to come to the hospital.

Physical Examination. General appearance, fairly well nourished, muddy-brown complexion.

Nose, negative, except hypertrophy of left inferior turbinate.

Mouth, large buried tonsils. Teeth, fair, pyorrhea; no sponginess of gums. Pharynx, negative.

Bronchoscopy (performed by Dr. Yankauer, after the patient had stopped bleeding) showed nothing that could throw light on the patient's complaint.

Lungs, slight dullness at both apices. No significant changes in breath sounds. No râles. Roentgenologic examination of lungs negative (Dr. Jaches and Dr. Wessler).

Heart, negative.

The abdomen, extremities, and genitals present nothing worthy of note.

Blood examination, hemoglobin 73 per cent, erythrocytes 4,200,000, leucocytes 12,000. Differential count, polymorphonuclear neutrophiles, 77 per cent; lymphocytes, 22 per cent; eosinophiles, 1 per cent. Platelets, 300,000. Bleeding time, four minutes. Coagulation time (test-tube method), five minutes. Wassermann reaction, negative. Urine, negative.

October 17–18, ½ mgm. tuberculin (old) given subcutaneously; no febrile reaction; no râles.

October 20–21, 1 mgm. old tuberculin given subcutaneously. Temperature rose from 98.4° F. to 99.6° F.; no general symptoms developed and no evidences of focal or local reaction. Tests with higher amounts of tuberculin could not be made, because the patient would not stay in the hospital any longer, as he did not feel that he was an invalid. During his stay of eleven days the temperature ran always between 98° and 99.6° F. During the first five or six days, he expectorated a great deal of dark, frothy, bloody fluid (about a pint jar full a day). The sputum was repeatedly searched for tubercle bacilli, but none was ever found.

On February 11, 1918, the patient returned for a physical examination, the result of which was entirely negative (E. L.). Weight 171 pounds. Systolic blood pressure 140; diastolic 85. He was referred to Dr. Alfred Braun for examination of the nose and throat, the result of which was as follows: Deviation of the nasal septum to the right. Hypertrophied tonsils and adenoids. Slight redness and thickening of the vocal cords, due to a mild chronic catarrhal laryngitis. Upper part of trachea is normal. There are no dilated vessels in any portion of the upper respiratory tract.

Case II.[1] E. R. (sister of first patient); age thirty years; married; housewife; admitted to the hospital, for observation, to the service of Dr. Brill, November 24, 1916; discharged November 25, 1916. This patient, like the other members of the family, refused to stay under observation for a period sufficiently long for us to carry out the investigations which we had planned.

She has two children nine and seven years of age, both healthy. Except for hemoptyses, she had never been seriously ill. She states that for most of her life she had a tendency to "catch cold," and develop a hoarse voice. She coughed up blood for the first time at the age of twelve, not having another attack until sixteen. Since then the attacks have come on at irregular intervals, sometimes skipping several years. When they occur she usually bleeds for hours at a time. She has bled three times during the last year, the attacks never lasting for more than one day. She always feels a tickling sensation a day or two before an hemoptysis, so that she can almost always foretell it. The blood which is brought up is bright red in color.

Nine years ago, after her first childbirth, she was for a time in poor condition, and thin; otherwise she has always been stout and vigorous. She has been repeatedly examined by physicians, some of whom suspected tuberculosis. Her sputum has been examined twice (three and four years ago) with negative results. Her last hemorrhage occurred in August, 1916. On the whole, her hemorrhages are mild as compared with those of her brothers R. W. and L. W.

Physical examination. Patient is stout, well nourished. Heart and lungs, negative. Larynx, negative. Bronchoscopy (Dr. Yankauer) failed to show anything that could account for the hemorrhages. There was no sputum to examine. The tuberculin test could not be done. The roentgenologic examination of the chest (Dr. Jaches) gave no evidence of any lung disease. Wassermann reaction negative.

On February 11, 1918, she returned for a physical examination, the result of which was negative (E. L.). Weight 177 pounds. Systolic blood pressure 140; diastolic 80. She was referred to Dr. Alfred Braun for examination of the nose and throat, the result of which was as follows: Small amount of adenoid tissue in the naso-pharynx. Slight thickening of the mucous membrane of the posterior commissure of the larynx, due to chronic catarrhal laryngitis. The upper portion of the trachea is normal. There are no dilated vessels in any portion of the upper respiratory tract.

Case III.[1] R. W. (cousin of first patient); age twenty-three years; operator; single; examined November 24, 1916. He had typhoid fever many years ago, and was suspected of having heart trouble at one time.

While at work, 2½ months ago, he suddenly expectorated blood. The bleeding lasted four days, but was not profuse—half a glass of blood in the whole time. He coughs a good deal for the last five or six years.

Physical Examination. Patient is lean with a pasty complexion. Chest asymmetrical; lungs, heart, and larynx negative.

On February 11, 1918, he returned for a physical examination, the result of which was as follows: Lungs, slight dullness at the right apex, somewhat increased voice and breathing; scoliosis to the right in the upper dorsal region, as a result of which there is a prominence in the region of the scapula, extending down to its upper third. Heart, negative. Weight 118.2. Systolic blood pressure 105, diastolic 80. Referred to Dr. Alfred Braun for examination of the nose and throat, the result of which was as follows: Acute pansinusitis, with pus in both middle and superior meati. No evidence of chronic sinusitis. Slight redness of the vocal cords, due to mild chronic catarrhal laryngitis. Upper portion of the trachea normal. No dilated vessels in any portion of the upper respiratory tract.

On December 23, 1918, we heard from Dr. Solomon S. Lubin, the family physician, through whose kindness it has been possible for us to remain in touch with this family. The family had continued having occasional hemorrhages, and none of the members of it had developed any signs or symptoms of tuberculosis. We have thus been in touch with this family for over two years, and we feel confident that tuberculosis can be excluded as the cause of the hemorrhages.

The only comparable disease with which we are acquainted is the Idiopathic Family Hematuria described in Apert's "Traité des Maladies Familiales et des Maladies Congénitales," from which the following notes were obtained.

This disease is well established by the observations of Atlee and of Guthrie. Atlee observed three sisters, all of whom suffered from attacks of hematuria. The observations of Guthrie are more convincing. In a family consisting of sixteen persons in two generations, twelve, five males and seven females (see chart in Apert's volume), presented from the time of birth attacks of hematuria recurring at irregular intervals.[2] The hematuria occurred after several hours of fever, stiffness, and lumbar pain. Occasionally a chilling or a digestive upset could be blamed for its production; most frequently it was absolutely spontaneous.

During the first days the urine is dark red. Later the color di-

[2] Paris, 1907, p. 288.

Circles = Females; Squares = Males; * = in Europe; no Details Obtainable. Shading Indicates Bleeders. The Numbers Inscribed in Squares or Circles Represent the Present Age of Each Individual. The Numbers above Squares or Circles Refer to Numerals in the Text; the Roman Numerals (I, II, III) Indicate Individuals Actually Examined by Us, the Arabic Figures (1, 2, 3) Bleeders That Were Not Available for Examination.

minishes in intensity, but does not disappear completely for a week to a month. Microscopic examination of the urine shows red blood cells in a number proportional to the color.

In the intervals between the crises the health is perfect and the urine analysis shows nothing peculiar. The patients are not subject to edema or to hemorrhages other than hematuria. They are not hemophiliacs, and never have suffered from purpura. They give no evidence of uric acid diathesis, nor of oxaluria, urticaria, erythema, or cyanosis of the extremities. Hematuria is the only morbid phenomenon.

PULMONARY ABSCESS

AN ANALYSIS OF ONE HUNDRED CASES, WITH SPECIAL REFERENCE TO CERTAIN ASPECTS OF ETIOLOGY, DIAGNOSIS, PROGNOSIS, INDICATIONS FOR AND RESULTS OF OPERATION

By Frederick T. Lord, M.D., Boston, Mass.

THE 100 cases included in this series comprise for the most part the more recent examples of abscess which have entered the wards of the Massachusetts General Hospital, or which I have seen in consultation outside the hospital. No attempt has been made to make the difficult distinction between abscess and gangrene. An effort has been made to follow the cases to their termination in order to obtain a more complete picture of the disease and the results which may be expected from operation. Ninety-one of the 100 cases have been followed to their termination either in death or present condition from one to ten years after discharge. Only cases in which pulmonary tuberculosis was apparently excluded are considered, but in two of the series tubercle bacilli later appeared in the sputum.

Etiology. Emphasis need be placed on only one group of cases—a group which has of recent years grown in importance and to which physicians should pay greater attention. In 25 cases, or 1 out of every 4, the cause may be definitely traced to an operation about the upper respiratory tract. The pulmonary abscess followed operation about the mouth for cancer of the jaw, lip, and tongue, in 1 case each, the removal of tonsils or tonsils and adenoids in 12 cases, the incision of peritonsillar abscess in 1 case, and the removal of teeth in 9 cases.

The history in certain instances indicates that the pulmonary suppuration is due to the aspiration into the deeper parts of the respiratory tract of blood, tissue, or infected material, and is followed by pulmonary manifestations usually within from one to four days after operation. Although the development of abscess after such operations is not wholly avoidable, the danger may be diminished by greater care in the performance of the operation.

DIAGNOSIS. There are in general five cardinal indications of pulmonary abscess: (1) Foul sputum and foul breath, (2) cough and explosive expectoration, (3) elastic tissue, with alveolar arrangement, in the sputum, (4) dullness on percussion over a circumscribed area, and (5) the demonstration by *x*-ray examination of a cavity with fluid level. These indications may be further elaborated as follows.

(1) *Foul Breath and Foul Sputum.* A bad taste in the mouth may be the first intimation. Foul breath may be noted only at the end of a paroxysm of cough. The breath may be foul and the sputum not offensive. Considerable care may be necessary to detect the bad odor. Attention should be paid to the expired air at the end of a coughing spell. The odor varies from slightly musty to foul or horribly offensive. In very rare instances the sputum and the breath are not malodorous, and the absence of bad odor is, therefore, not an assurance against abscess, but in the presence of foul sputum and foul breath, pulmonary abscess or gangrene is almost invariably present.

(2) *Cough and Expectoration.* It should be noted that the cough and expectoration, aside from the odor, usually present no striking features, and there is no distinctive gross character to the sputum. In the absence of signs of empyema, however, the sudden explosive expectoration of a considerable amount of foul pus as an initial manifestation, is an almost conclusive sign of abscess. Explosive expectoration is unusual, however, and was noted in only eleven cases in this series. As a later manifestation, the evacuation of a considerable amount of sputum one or more times daily with relative or complete freedom from cough in the intervals may occur, and was observed in four instances. Mild or severe septic manifestations may follow periods of incomplete evacuation.

(3) *Elastic Tissue in the Sputum.* Too little attention is commonly paid to this important sign of pulmonary destructive lesions. Microscopic particles of elastic tissue are much more common than shreds of pulmonary substance. Sedimentation and appropriate staining largely increase the number of positive cases. Caution should be observed to ascribe a pulmonary source only to those particles of elastic tissue which have an alveolar arrangement.

The exclusion of pulmonary tuberculosis is of paramount importance in the selection of cases for operation. Inasmuch as tuber-

culous lesions which have progressed to the stage of the expectoration of sputum containing elastic tissue are likely also to show tubercle bacilli, the demonstration of elastic tissue and the failure to find tubercle bacilli in repeated examination are strong assurance against the tuberculous nature of the disturbance.

(4) *Physical Signs.* In a small proportion of cases with small or deep-seated processes, there are no physical signs of abscess, which is first disclosed by *x*-ray examination or autopsy. Dullness on percussion is common to all cases with positive physical findings, and is the most important single sign. Signs other than dullness are variable, but in general conform to those which may be expected in the presence of encapsulated fluid within the chest, i.e., diminished voice, whisper, and tactile fremitus. Râles usually accompany the more recent and active destructive lesions due to pneumonia about the abscess. In certain abscesses, however, there is very little reactive neighborhood-inflammation, and in such cases no râles may be heard. The breathing is usually bronchial and of diminished intensity. A marked increase in voice, whisper, and tactile fremitus may be present over large superficial abscesses communicating freely with the bronchi.

The signs of cavity are infrequent, and were noted in only eighteen cases. Amphoric breathing is the most common single sign. Tympany on percussion, cracked-pot resonance, and metallic râles are occasionally noted. Succussion sound was not found in any case of uncomplicated abscess in this series.

Even large abscesses may give only slight signs. Slight dullness over the involved region was the only suggestive deviation from the normal in Case XVIII, yet *x*-ray (Plate III) showed a large area of increased density with central area of diminished radiance. Only slight dullness, slightly diminished and bronchial breathing with slight increase of voice and diminished tactile fremitus without râles were present in Case XV. Autopsy (Plate I) showed a closed cavity 14 x 11 x 2.5 cm. full of pus. In Case XXXVIII the left lung showed much diminished vesicular breathing throughout, thus pointing to it as the site of the process. Only slight dullness, slight increase of whisper, and tactile fremitus without other signs could be demonstrated over the site of an abscess deep in the substance of the left upper lobe, found at autopsy following an unsuccessful

operation to contain 8 ounces of pus. Slight dullness, diminished breathing, and numerous fine consonating râles over an area below the angle of the left scapula were the only signs in Case XXV. *X*-ray confirmed by operation and later by autopsy showed a deep-seated abscess of the left lower lobe, 4½ cm. in diameter (Plate IV).

(5) *X-ray Examination.* This is an indispensable method and an important educational measure for the physician, realized to its full extent only when physical examinations are first recorded for later comparison with the *x*-ray findings. The *x*-ray may then confirm the physical findings or disclose deep processes otherwise difficult or impossible of demonstration. It is a valuable means of excluding certain cases unfavorable for operation, and an important guide to the surgeon if operation is undertaken.

A frequent mistake is to neglect the importance of *x*-ray examination with the patient in the upright (Plate V) rather than the prone position (Plate VI). Cavities with free fluid can be detected only in the upright posture. Radioscopic examination at frequent intervals may lead to the detection of abscess before the obscuration of the picture by a complicating involvement of the pleura. In Case XXV, an abscess behind the heart was first demonstrated as an empty cavity at the third *x*-ray examination (Plate IV), previous plates having failed to disclose the cavity full of pus, on account of the overlying shadow of the heart.

The affected lung may show some diminished radiance throughout with narrowing of the intercostal spaces and elevation of the diaphragm in consequence of atelectasis.

The abscess itself usually appears as an irregularly rounded area of even density, its margins sharply defined or fading gradually into the lung markings. More definite findings are exceptional, but there are several groups of cases with somewhat different appearances.

At times a rarefied central area or areas may be seen in the midst of a dense region. Such an appearance is not conclusive evidence of cavity, as it may represent a less dense infiltration or partial resolution within a pneumonic area. Valuable additional evidence regarding the cause of such an appearance may be afforded by *x*-ray examination before and after efforts at evacuation by cough.

If a central area is repeatedly absent before and present after evacuation of a considerable amount of pus, a more certain conclusion may be drawn. In Case XVIII the even density of a full abscess (Plate II) was replaced by a "doughnut" shadow after evacuation (Plate III).

In rare instances, as in Cases XV, XXX, and XXXVIII, the limiting wall of an abscess presents a dense, thin, sharply defined circle of density with little or no diminished radiance in the surrounding tissue. In such cases it may be impossible to feel the limiting wall of the abscess cavity at operation.

The most distinctive appearance is that of a dense area of increased density of variable but usually considerable width, inclosing a rarefied area above and a dense area below, with constant fluid level (Plate V). Such an appearance is distinctive of a cavity partially filled with fluid. Such cavities were demonstrated in twelve cases in this series, and would doubtless have been found in a larger number if plates with the patient upright had been taken in all cases.

In cases in which there is mottled increase of density, abscesses, if present, are likely to be small and multiple and unfavorable for operation in view of the surgical risk and small chance of notable benefit. In Cases XII and XXIX, for example, operative exploration of such an area (Plates VII and VIII) led to the evacuation of only a small cavity. It is important to become familiar with the degree of even density sufficient to warrant interference and to appreciate the significance of uneven mottling as a deterrent to operation. The distinction between these two types can best be made by the comparison of *x*-ray plates with the findings at autopsy on the fatal cases. A comparison of Plate VII with Plates II, III, V, and VI, will serve to suggest the different appearance in the two groups.

X-ray examination may be negative in the presence of abscess below the level of the dome of the diaphragm or behind the shadow of the heart (Plate IV). Lateral views are difficult of interpretation, but may be of assistance in such cases.

Outlook in Unoperated Cases. Of 38 unoperated cases, 24 died—a mortality of 63 per cent—and 14 are alive or not traced.

Inevitable Fatalities. The gravity of the situation from the presence of menacing complications, the poor general condition of the patients, and the small size and multiple character of the abscesses, excluded 20 of the

24 fatal cases from surgical consideration. One of these is reported to have died of pulmonary tuberculosis after discharge.

Medical Failures. Earlier investigation might have saved 4 of the unoperated and fatal cases.

Spontaneous Recoveries. Of 14 unoperated cases, 7 spontaneously recovered. They represent an important group which justifies delay in the resort to operation in certain cases. All were relatively mild with a short previous duration. The illness lasted from one to two months in 6, and eight months in the seventh. Recovery was complete in all.

Partial or No Relief. The remaining 7 unoperated cases continued to cough and expectorate at their discharge; 2 are similarly troubled after two and five years respectively; 5 cannot be traced.

Outlook in Operated Cases. Of 62 operated cases, 35 died in hospital or after discharge—a mortality of 56 per cent. Reviewing these cases from the standpoint of an internist, I may be permitted to find extenuating circumstances for the lack of success in certain instances.

Inevitable Fatalities. Twenty-nine, 46 per cent, of the 35 seem to belong to this group. Some hopeful prospect of success in the face of multiple cavities, complicating pneumonia, brain, liver, or subdiaphragmatic abscess, general sepsis, myocardial disease, or carcinoma, led to the unsuccessful attempt at operative relief in the vain effort to save life, but in 3, earlier operation with the patient in better general condition would probably have succeeded. One patient with a history of previous hemoptysis died from a recurrence of the bleeding after operation. Three died after discharge, 1 seven years later in a railroad accident, a second sixteen months later of pulmonary tuberculosis, and the third one year later of an unknown cause.

Surgical Failures. Nine, 14 per cent, may be put in this category. Three succumbed to post-operative hemorrhage, probably in consequence of the injury to granulation tissue about the abscess or the opening of blood vessels lining the wall or traversing the lumen of the abscess cavity. I have been an interested and anxious observer at many operations, and never see the surgeon search for the abscess with a sharp-pointed instrument without fear of disaster. One fatality occurred from the aspiration of infected pus during anesthesia. The maintenance, if possible, of such a position that the affected region is dependent during operation will diminish this danger. Previous evacuation of the abscess by cough is also a safeguard, but may increase the difficulty of locating the cavity at operation. In a fifth, exploration in the right paravertebral region was unsuccessful in locating a cavity of the right upper lobe (Plates V and VI). The patient never regained consciousness and died about eighteen hours after operation. Injury to the sympathetic nerve in the course of the operation is a possible explanation

A sixth died following an unsuccessful exploration of the left upper lobe in which, at autopsy, was found a thin-walled abscess containing 8 ounces of pus. The absence of induration about the abscess and failure to find it by palpation was in part responsible for the operative failure. All of these six patients would probably have died without operation, but the mortality of the operation may be estimated at 6 in 62 cases, or 9 per cent.

In 3, the abscess was not found at operation, and these cases also must be classed as operative failures, though without the grave consequences in the preceding group. The patients survived the operation without apparent detriment. Two have persistent symptoms of undiminished severity and the third cannot be traced. Sufficiently accurate localization of the process to enable the surgeon to find it is a troublesome matter in certain cases. There is a hopeful prospect of progress, however, in difficult cases by the addition of the improved portable *x*-ray apparatus to the armament of the surgeon, who may then guide his exploration by means of the fluoroscopic screen.

Complete Surgical Success. Following the finding and evacuation of the abscess, 10, 16 per cent, were completely cured, though 1 still has a discharging sinus, but no cough or expectoration. These patients have been followed from one to five years. Seven would probably have died without operation.

A brilliant success, accomplished only after overcoming many difficulties, should be noted in further detail in 1 courageous patient. Case XXXI was a woman of forty-three, who consulted me in 1914 with a history of chill, fever, and weakness nine months before, followed one week later by a sudden and violent paroxysm of cough, lasting 1½ hours, without expectoration, but accompanied by a sensation of bad odor and bad taste in the mouth. The paroxysmal cough without expectoration recurred about six times each day after this, with slight cough in the intervals. Irregularly elevated temperature was noted in the next seven weeks. Seven months before I saw her she had sudden intense pain in the left axillary region and a week later a gush from the mouth of an ounce of green, foul-smelling pus, with cough. Cough and purulent expectoration, amounting to 3 ounces a day, and fever of 99.4° to 100°, persisted since. Examination, negative other than the pulmonary findings, showed, in the left back between the seventh and tenth ribs in the paravertebral region, dullness, slightly increased and bronchial breathing, increase of voice (without egophony), increased whisper and much diminished but not absent tactile fremitus. The white count was 10,600, of which 85 per cent were polynuclears and 15 per cent lymphocytes. The sputum was purulent and of a slightly musty odor. No tubercle bacilli, actino-

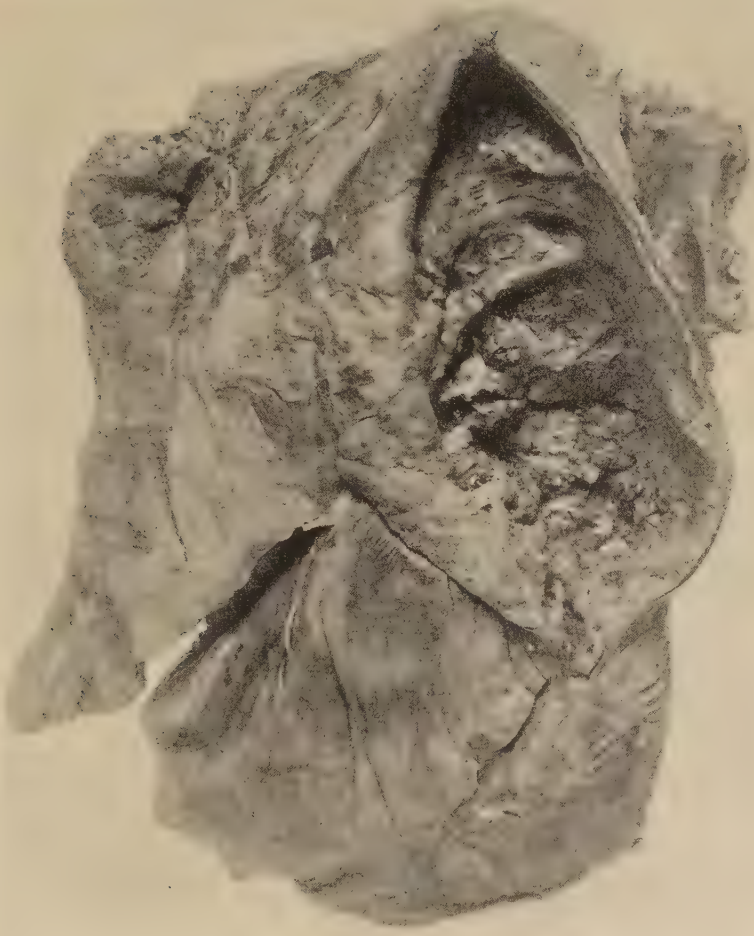

PLATE I. CASE XV. LARGE ABSCESS OF LEFT LUNG.

Involving the Upper and Lower Lobes, 14 cm. Long, 11 cm. Wide, and 2.5 cm. Deep. The Cavity was Full of Purulent and Necrotic Material. No Fibrous Induration was Noted along the Wall of the Abscess, and no Areas of Consolidation in Either Lung.

PLATE II. CASE XVII. FULL ABSCESS OF UPPER RIGHT LOBE.
Evenly Dense Rounded Shadow in Right Upper Lobe. Contrast with Plate III.

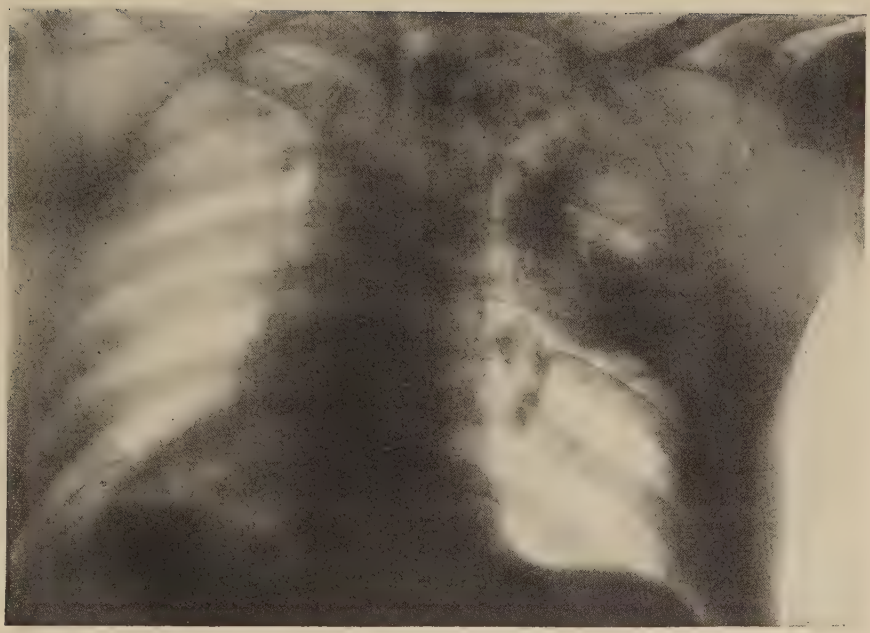

PLATE III. CASE XVIII. EMPTY ABSCESS OF RIGHT UPPER LOBE.

Wide, Evenly Dense Zone, with Central Area of Diminished Radiance. Contrast with Plate II.

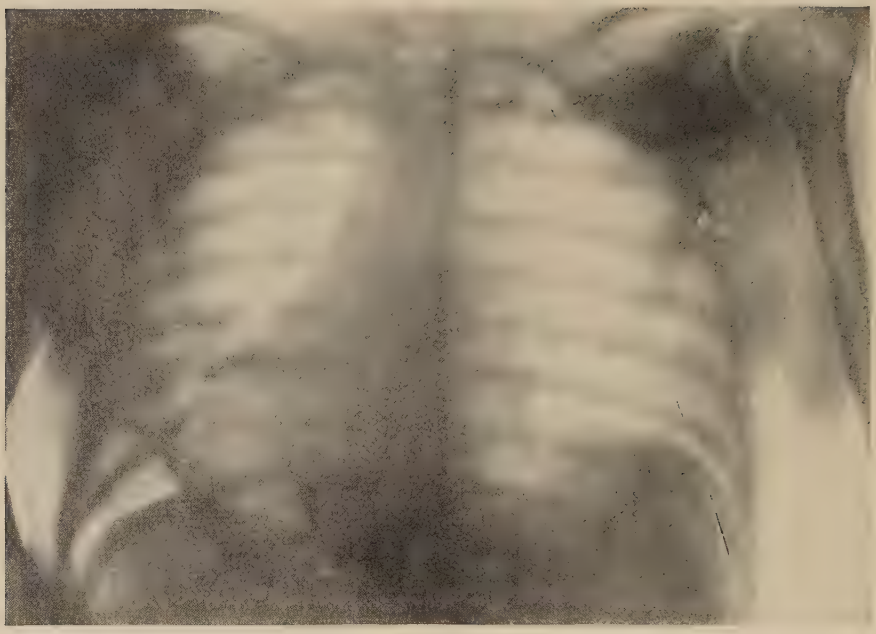

PLATE IV. CASE XXV. ABSCESS OF LEFT LOWER LOBE, WITH CAVITY FOUND AT AUTOPSY TO BE 4½ CM. IN DIAMETER.

Previous Roentgenograms Failed to Show the Abscess Owing to the Density of the Overlying Heart Shadow. In this Plate the Diminished Density of the Central Portion and the Circular Zone of Increased Density are Brought about by the Evacuation of the Contents of the Abscess by Cough.

PLATE V. CASE XLII. ABSCESS OF UPPER RIGHT LOBE.

The Examination with the Patient in the Upright Position. Area of Much Increased Density Containing a Central Bright Area, Showing Fluid Level. Contrast with Plate VI.

PLATE VI. CASE XLII. ABSCESS OF RIGHT UPPER LOBE.

Examination with the Patient in the Prone Position. Area of Much Increased and even Density without Central Bright Area, Owing to the Prone Position. Contrast with Plate V.

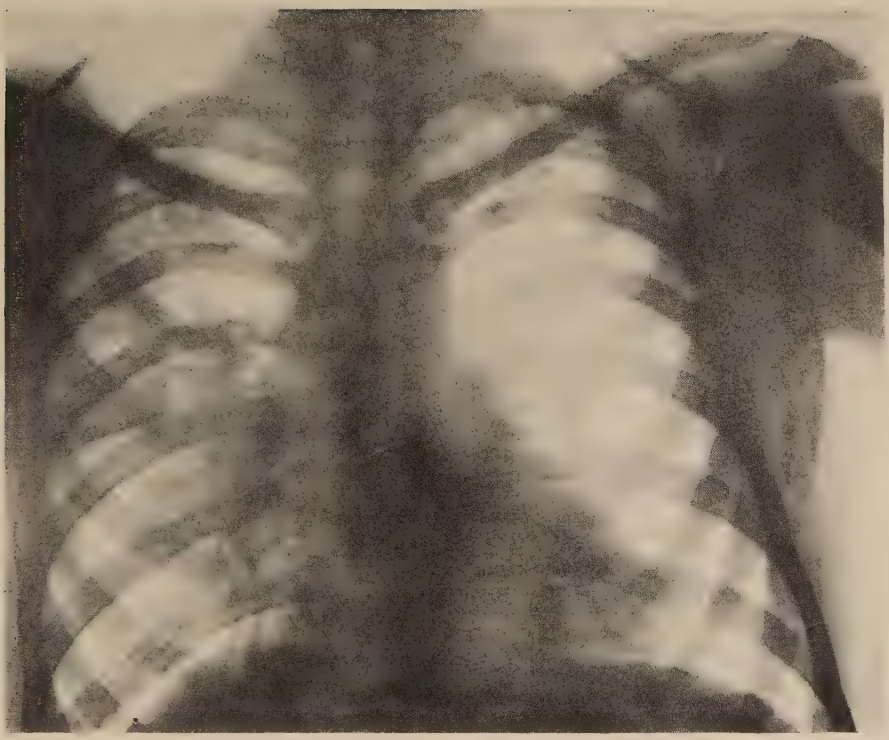

PLATE VII. CASE XII. MOTTLED DULLNESS AT RIGHT LUNG ROOT AND OUTER PORTION OF RIGHT UPPER LOBE.

The Thinness and Uneven Quality of the Increased Density Suggest the Absence of Other than Small Cavities Surrounded by Areas of Broncho-Pneumonia. Operation Disclosed Only a Small Cavity. Contrast with the Greater Density in Plates II, III, V and VI.

PLATE VIII. CASE XXIX. EXTENSIVE MOTTLED DISEASE FROM THE APEX TO THE SIXTH RIB, WITH SMALL CENTRAL BRIGHT AREA.

The Appearance is Somewhat More Favorable for Operation than that in the Previous Plate (Plate VII), but only a Small Cavity was Found at Operation.

myces, blastomyces, or streptothrices were seen. Elastic tissue was present. *X*-ray examination showed in the left chest a well-circumscribed, evenly dense area corresponding in position to the findings on physical examination. Operation by Dr. C. L. Scudder in first and second stages in October, 1914, evacuated about 1 ounce of foul pus from the abscess. A left pneumothorax complicated the convalescence and a discharging sinus followed. Cough and expectoration, though diminished, still persisted. A third operation was performed in November, 1915. A fourth operation in May, 1916, evacuated a cavity about the size of the middle finger and disclosed two dilated bronchi leading from it, and finally led to complete and permanent cure.

Incomplete Surgical Success. In 14, 22 per cent, drainage of the abscess was followed by incomplete relief; 9 would probably have died without operation. All but 3 of the 14 in this group have been followed from one to five years, and all those followed continue to cough and expectorate. Partial failure may be ascribed to the extent of the complicative pneumonia and pulmonary induration, multiplicity of abscesses, many of which are inaccessible and fail to drain into the field of operation, and dilatation of the bronchi. Complete or partial success may, therefore, be noted in 38 per cent.

Theoretical Outlook in Unoperated Abscess. The expectation of life for patients with pulmonary abscess has never been accurately determined. It cannot be estimated from a series of cases in the preoperative period, because of inadequate exclusion of tuberculosis, failure to establish the presence of a destructive lesion by finding elastic tissue in the sputum, and the absence of *x*-ray examinations. An estimate of the theoretical mortality from the present group is only approximately accurate. Excluding from consideration the 2 cases fatal from pulmonary tuberculosis and 1 dying from accident, 97 are left for consideration. The mortality without operation may then be estimated by the sum of 24 deaths in the unoperated and 32 in the operated series, plus the 16 which would probably have ended fatally without operation in the operated group, or 72 deaths in 97 cases—a mortality of at least 74 per cent. Even this is probably too favorable a showing, since in the estimate the 9 cases not traced after discharge are counted, it may be erroneously, as living.

Of the remaining 25 patients, 18 had persistent symptoms at the time of discharge, and of these 9 cannot be traced, but a continued disability is probable if they are still alive. A permanent and distressing damage may, therefore, be calculated for the 18, or 18 per cent, who escape death for a longer or shorter period. The fortunate few who are left for consideration are the 7, or 7 per cent, who spontaneously recovered.

Influence of the Previous Duration on the Chances of Operative Relief. Our previous experience seemed to indicate an important difference between the acute and chronic cases with respect to the expectation of relief by operation. This seems in general true, and the acute cases are more favorable for operation. Of the 10 complete cures by operation, 7 had a duration of three to seven weeks. The remaining 3 cases had had a duration of nine months to three years. A consideration of the duration alone is not enough to influence the judgment concerning the desirability of operation. Owing to the greater likelihood of multiple lesions, hence greater chance of partial operative failure, more dense induration with the added risk of post-operative hemorrhage, and the septic complications likely to arise with the progress of time, it is highly desirable that an early decision be reached concerning operation.

Indications for Operation. While pulmonary abscess should always be regarded as a surgical affection, the chances of spontaneous and complete recovery, as in 7 instances in this series, must always be taken into account in selecting cases for operation. With rare exceptions spontaneous recovery is not to be expected, however, in other than mild cases with a short previous duration. While there should be some restraint against an immediate resort to operation in such cases, yet the permanent and distressing disability in the chronic cases, the danger of the development of induration about the abscess, multiplicity of pulmonary lesions, other local or general septic complications and the consequent diminishing chance of cure with the lapse of time should influence the decision.

X-ray examination is one of the most important guides to operative interference. Mottled increase of density is not favorable for operative relief. Evenly dense, circumscribed shadows, with or without central areas of diminished density or the appearance of fluid level, are more favorable.

On the clinical features in connection with the *x*-ray examination a decision must be made. Tuberculosis must be adequately excluded. A short previous duration, pure purulent (not foul) sputum, without abundant elastic tissue, only mild symptoms of sepsis, and a small process justify delay and the estimate of progress during a short period of observation. Unless recovery or marked improvement occurs in such cases in three to four weeks, operation should be considered. Operation is indicated, on the other hand, without regard to the

previous duration, with foul sputum containing an abundance of lung tissue and marked symptoms of sepsis. Multiple areas are not necessarily a contraindication, but greatly increase the operative risk. In cases which have lasted for months or years the exigencies of the individual case and the chances of operative relief determine the propriety of surgical intervention. Much care must be exercised in selecting the cases for operation to exclude those with diffuse broncho-pulmonary infection, multiple losses of pulmonary substance, and probable bronchiectasis, as unfavorable until such radical measures as lobectomy offer greater promise, and choose the sharply localized abscesses as offering a greater prospect of surgical success.

[END OF VOL. I]